SURGERY

VOL. 36 OCTOBER, 1954 NO. 4

Original Communications

LIPOSARCOMA

A STUDY OF 105 CASES

GEORGE T. PACK, M.D., AND JOHN C. PIERSON, M.D., NEW YORK, N. Y.

(From the Memorial Cancer Center)

DURING the last twenty-five years all malignant lipogenic tumors at the Memorial Cancer Center have been subject to the group judgment and treatment of the Mixed Tumor Service. This opportunity has permitted a survey of the largest group of these sarcomas ever studied and an application of principles of treatment under uniform guidance. The 105 cases of liposarcoma constitute 14.6 per cent of all sarcomas of the soft somatic tissues, being third in frequency and exceeded in incidence only by the group of sarcomas classified as of undetermined histogenesis (35.7 per cent) and by rhabdomyosarcomas (15.3 per cent). From 1928 to 1953, we diagnosed and treated about the same number of liposarcomas in each five-year period, which at least suggests that the clinical and microscopic diagnosis of liposarcoma has not been influenced by waves of diagnostic popularity, as occurs with some tumors. Since Virchow in 1857 first recorded a malignant tumor of fat tissue, we have found only one report of a sizable series, that of A. P. Stout, who published an analysis of forty-one cases of liposarcoma from the records of the Department of Surgical Pathology, Columbia University, during thirty-seven years. (Table I.)

Sex Distribution.—Stout found liposarcomas to occur twice as commonly in males as in females. In our personal series, the distribution between the sexes was males 56.5 per cent, and females 43.5 per cent. This disparity is contrary to the well-known greater frequency (73 per cent) of benign lipomas in females (Adair, Pack, and Farrior).

Regional Distribution of Liposarcomas.—The benign lipomas are more commonly situated in subcutaneous tissues, but the malignant lipogenic tumors seem to have a greater predilection for the deeper soft tissues. Liposarcomas may occur wherever fat is present. The lower extremity including the foot (2.7 per cent), the leg (6.7 per cent), the thigh (40 per cent), the buttock (5.3 per cent), and the groin (8 per cent) is the composite site for 62.7 per

Received for publication Feb. 4, 1954.

cent of all liposarcomas in this series, as compared with only 24 per cent developing in the upper limb, where they are distributed between the arm (16 per cent) and the shoulder (8 per cent). The remaining 13.3 per cent involves the retroperitoneum and trunk. In the extremities, the liposarcomas seem to be intimately associated with the intermuscular, deep fascial, and periarticular tissues.

TABLE I. MALIGNANT TUMORS OF THE SOFT SOMATIC TISSUES: DISTRIBUTION ACCORDING TO HISTOLOGIC TYPE AND SEX OF PATIENT

HISTOLOGIC TYPE OF TUMOR	TOTAL CASES	PER CENT	MALES		FEMALES	
			NUMBER	PER CENT	NUMBER	PER CENT
Total cases	717	100.0	405	56.5	312	43.5
Sarcoma of undetermined histogenesis	251	35.0	138	55.0	113	45.0
Rhabdomyosarcoma	110	15.3	65	59.1	45	40.9
Liposarcoma	105	14.6	59	56.2	46	43.8
Synovioma	60	8.4	31	51.7	29	48.3
Kaposi's sarcoma	48	6.7	41	85.4	7	14.6
Malignant neurilemmoma	46	6.4	23	50.0	23	50.0
Fibrosarcoma	39	5.4	16	41.0	23	58.9
Dermatofibrosarcoma protuberans	39	5.4	24	61.5	15	38.5
Angiosarcoma	19	2.6	8	42.1	11	57.9

Liposarcoma of bone: These tumors are excluded from the present series as they are not primarily of soft-part origin. Dr. James Ewing in 1928 first described a liposarcoma developing in the bone marrow. In 1931 his associate, Dr. Fred W. Stewart, reported three such cases with characteristic histologic structure and fatal course. The identity of this tumor was challenged by the late W. G. Barnard, and Arthur Purdy Stout acknowledged that they do appear different from the liposarcomas originating in other locations.

Relation of liposarcoma to benign lipoma: The possibility of malignant lipogenic tumors developing in pre-existing benign lipomas is to be admitted, but the majority of liposarcomas undoubtedly occur de novo. Lipomas are not seen as a constant accompaniment of liposarcomas. Stephen S. Sternberg has recently reported an authentic case of liposarcoma arising within a subcutaneous lipoma. There have been two bona fide instances in our own series of cases. In one man, a subcutaneous lipomatous tumor on the anterior aspect of the thigh grew slowly but to large proportions during the course of nineteen years; finally, a firm, orange-yellow, spherical lobule at the superior pole grew with great rapidity. The entire neoplasm was surgically dissected. Liposarcoma had developed in the degenerating xanthomatous superior lobule of the tumor. Another man with almost innumerable subcutaneous quiescent lipomas observed the phenomenally rapid growth of one in the precordial region. Within a few weeks it became fungating, infected, enormous, invasive, and exsanguinating. Treatment by combined irradiation and surgical excision resulted in an apparent cure during the past eight years.

The great frequency of lipomas and the rarity of liposarcomas would indicate that the percentage of lipomas undergoing malignant degeneration must be very low. On the Mixed Tumor Service, the ratio of benign lipomas to

liposarcomas is approximately 120 to 1. To verify the authenticity of a malignant change occurring in a benign lipoma, the pathologist should be able to trace the histologic relationship. The so-called "recurrent" lipoma may be improperly diagnosed. True, a portion of a multilobular lipoma may not have been removed originally, only to grow later, but others which recur rapidly and are found to contain foci of myxomatous tissue and cellular islands offer strong presumptive evidence that the lipogenic tumor was probably sarcomatous from the very beginning.

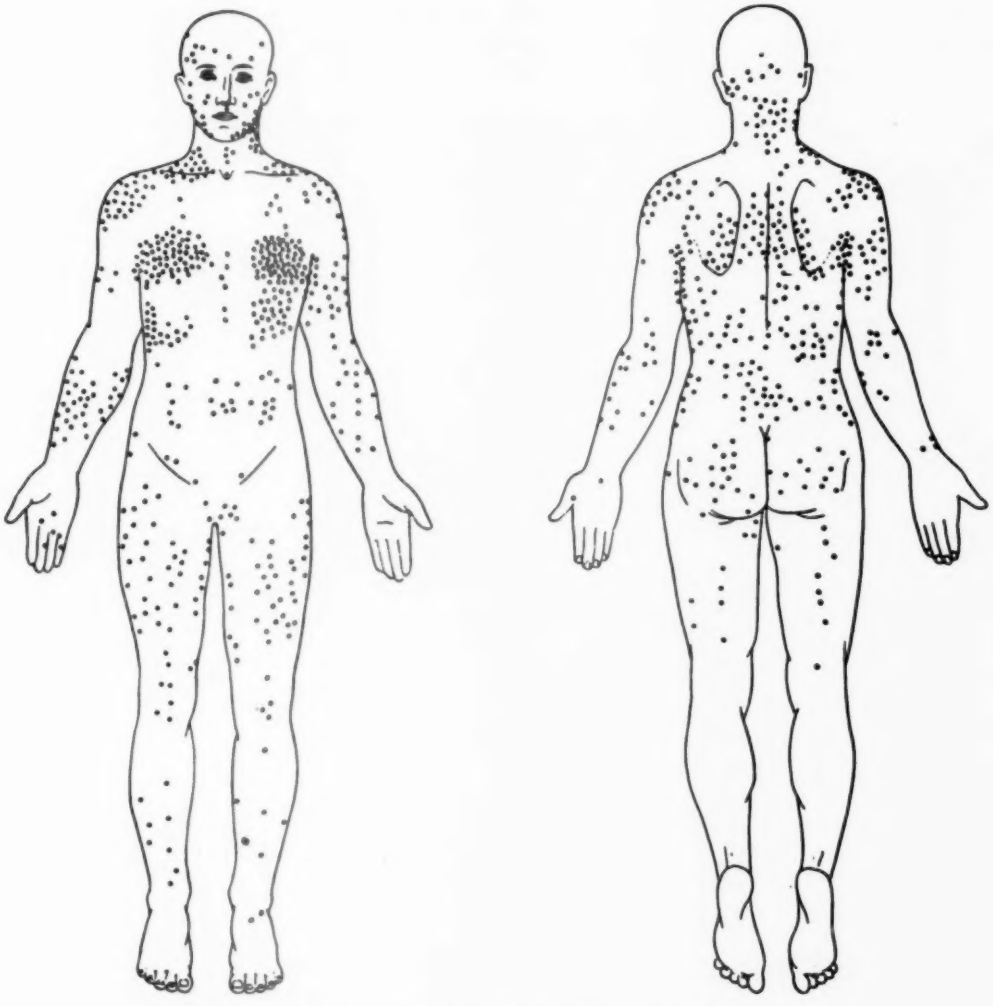


Fig. 1.—Scattergram. Regional distribution of benign lipomas.

Causative Factors.—Liposarcoma can be produced experimentally in laboratory animals, but the cause of these apparently spontaneous tumors in human beings remains unknown. Haagensen and Krehbiel used 1:2 benzpyrene, and provoked one liposarcoma in a mouse and four in guinea pigs. The importance of this observation is the evidence it presents that liposarcoma may arise from adult fat cells as a result of prolonged chemical irritation and

stimulation. James Ewing stated that "since traumatism to fat tissue is often followed by marked proliferation of fat cells and progressive productive inflammation, it is not unreasonable to assume that under special circumstances the proliferation may take on a malignant character." Although Ewing considered trauma a reasonable explanation for the origin of some subcutaneous liposarcomas of the adult cell type, Stout attributed to injury only a very minor role, which agrees with our point of view. Considering the innumerable bruises which 150,000,000 Americans sustain yearly, the likelihood of trauma causing liposarcoma must be quite remote. There have been a few instances in our experience wherein local injury with ecchymosis has preceded the appearance of this tumor at the site of injury. Such a case report is included here.

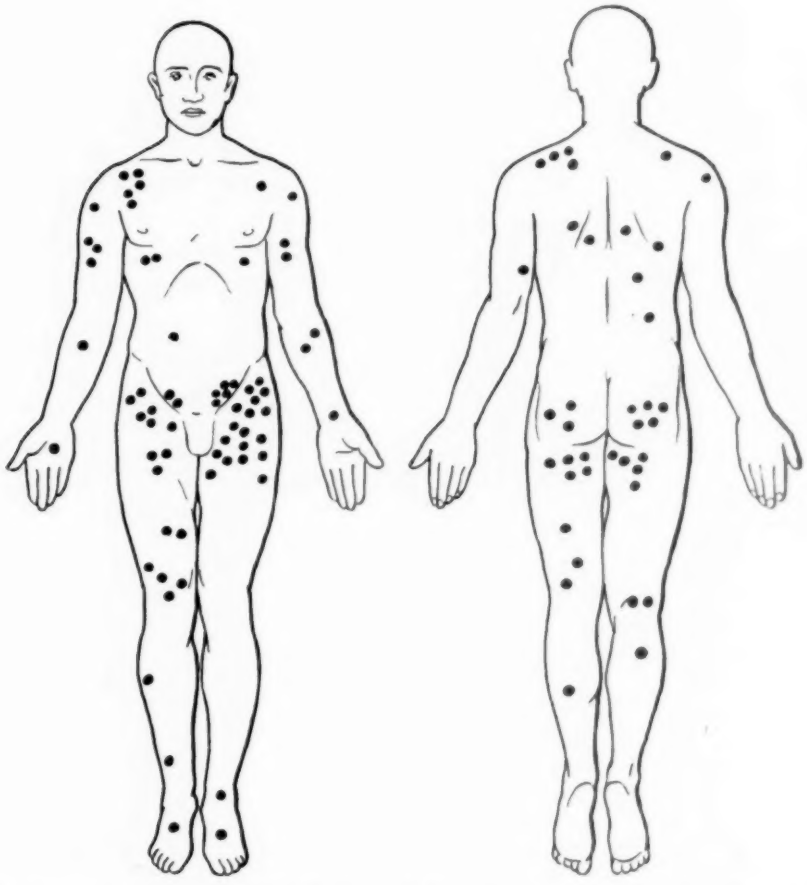


Fig. 2.—Scattergram. Regional distribution of liposarcoma (105 cases). Note incidence of involvement of thighs, buttocks, and shoulder girdle.

CASE 1. *Questionable Traumatic Origin of Liposarcoma.*—

A. B., a 34-year-old, white, single, female schoolteacher, was admitted to Memorial Hospital on May 31, 1937. In September, 1936, while riding a mule on her vacation, she was thrown, and the mule stepped on her upper inner left thigh. The mark of the mule's hoof was seen on the skin at the time of the injury, lacerating the thigh. A slight, tender swelling appeared beneath the site of the injury, but gradually disappeared following the

application of heat. This was diagnosed as a hematoma. There was, however, a residual scar in the skin at the site of the injury and dimpling of the skin over an underlying nodule. The thigh, which had been swollen from the hip to the knee, regained its normal size. She was well enough to engage in winter sports such as skiing and skating, and in March, 1937, had a general physical examination, at which time no residual abnormality in the injured thigh was found. Later that month she noticed a reappearance of the mass at the site of the injury. It gradually increased in size until May, 1937, when a local excision was attempted in a Western hospital. The tumor was found to be situated in the left thigh in the region of the left femoral trigone. It was described as an infiltrating myxomatous tumor adherent to the femoral vessels. Only a portion of the tumor was surgically removed. It was very vascular and bled profusely, requiring packing to control the hemorrhage. Following this operation, the patient received three x-ray treatments to each of three ports, one anterior, one posterior, and one lateral: the exact dose was not stated. She was sent across the continent with the packing still in the wound.

A.

Fig. 3.—*A*, Huge lipoma of nineteen years' duration. Xanthomatous degeneration. Liposarcoma developing at superior pole. Surgical dissection. Late pulmonary metastases.

Physical examination on May 31, 1937, at the Memorial Hospital revealed a well-nourished woman of 34 years, in good general health. In the region of the left thigh, over the region of Hunter's canal, was a linear wound with the sutures intact; the wound was not completely healed, and it discharged bloody serum. There was an indefinite mass, 10 by 12 cm., soft and compressible over the femoral vessels. The tumor did not seem to extend high in the femoral trigone, and the inguinal lymph nodes and femoral nodes were palpable but soft, suggesting adenitis only. There was good motor function of the thigh, although some atrophy of disuse. The pathologic diagnosis based on the submitted slide was myxoliposarcoma (Ewing).

Summary of treatment: While in the Memorial Hospital, from June 1 through 19, she received 152,000 mg. hr. of external irradiation over the site of the tumor, applied by a 4 Gm. radium element pack at 20 cm. radium-skin distance, 8 Gm. hr. daily. From July 13 to August 13, during a second admission, she received 80,000 mg. hr. to the left groin with the radium element pack. When she left the hospital in June, 1937, there was profuse discharge from the anterior thigh and an intense radiation reaction was beginning. On Aug. 9, 1937, she received high voltage x-ray therapy to the left thigh through two portals, anteromedial and anterolateral, employing the following factors: 198 kv., 0.5 cm. Cu filter, 70 cm. target-skin distance, field: 18 by 11 cm., 250 r daily to alternate ports for a total of 2,000 r to each portal. At no time during our observation was the tumor locally resectable, and in those years we had not started to perform hemipelvectomy for locally nonresectable tumors of this location.

B.

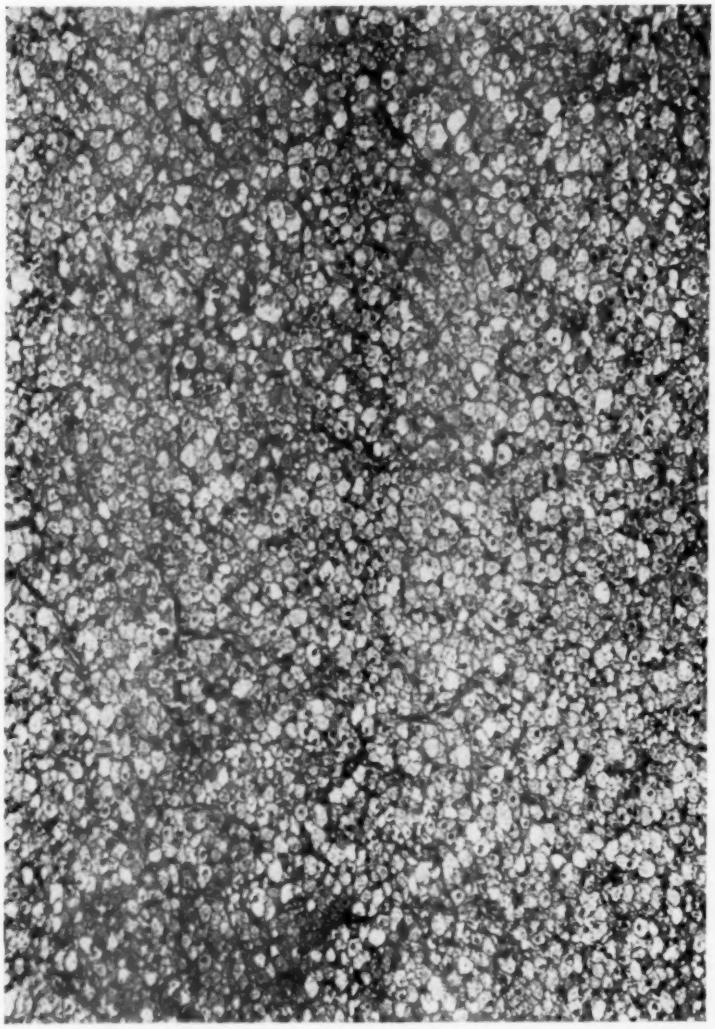
Fig. 3 (*Continued*).
B, Gross specimen of patient shown in *A*. Degenerating lipoma. Intratumoral hemorrhage. Solid liposarcoma at superior pole.

Repeated aspirations of the tumor were required because of the collection of enormous quantities of blood serum. On Aug. 12, 1937, she complained of pain in the left chest over the eighth rib; this pain was intensified by deep inspiration. An x-ray film of the chest two days later disclosed a dense shadow in the right upper lobe, suggesting metastasis. A previous film made July 10, 1937, was normal. The pulmonary metastases increased, and the patient developed strabismus in the left eye on the day of her death, Sept. 11, 1937.

Necropsy report :*

Anatomic diagnosis:

1. Liposarcoma of the left thigh.
2. Metastases to retroperitoneal and right supraclavicular nodes, lungs, pleura, mediastinum, diaphragm, heart, liver, adrenals, left kidney, and left ovary.
3. Hydrothorax.
4. Pulmonary atelectasis, edema, and congestion.
5. Myoma uteri.



C.

Fig. 3 (*Continued*).
C, Photomicrograph of xantholipomatous segment of tumor shown in Fig. 3, *A* and *B*.

Microscopic diagnosis:

1. General liposarcomatosis.
2. Persistent thymus.
3. Early acute hepatitis.
4. Thrombosis of the right adrenal artery.

*By Dr. Fred W. Stewart.

Comment.—The postulates governing the possible origin of a malignant tumor following a single trauma seem to have been fulfilled in this case. The authentic history of trauma, the physical evidence of injury, such as laceration and ecchymosis, the absorption of the hematoma, the development of the tumor at the exact site of injury, the interval between the date of the trauma and the appearance of the tumor, and so forth, all are in accordance with the accepted tenets of this theory. We cannot accept this doctrine of traumatic etiology for sarcomas of the soft somatic tissues, yet there does occasionally occur a case as related here wherein the sequence of events would be difficult to disprove in court.

Fig. 4.—Liposarcoma of chest wall, treated by surgical dissection and irradiation with eight-year definitive cure. Numerous subcutaneous lipomas.

Gross Anatomic Features of Liposarcoma.—The pseudoencapsulation of the average liposarcoma suggests its benignity and tempts the first surgeon unwisely to perform a simple enucleation. The primary liposarcoma is commonly situated deeply in the intermuscular or periarticular planes rather than in the subcutaneous location. The original delimited, multilobular tumor lies between, but does not invade, the muscles; this localization may explain the error of labeling these tumors "fascial sarcomas." The recurrent liposarcomas do have invasive propensities, and infiltrate muscle, fat tissue, and skin. In rare instances, the liposarcomas are of multicentric origin; two patients in this series had more than one primary liposarcoma. The fibrous septa divide the tumor lobules. Some liposarcomas are highly pigmented, varying from

yellow to orange-yellow and even brown, with or without evidence of intratumoral hemorrhage.

Histologic Features of Liposarcoma.—We shall present two classifications of liposarcoma, as outlined by James Ewing and Arthur Purdy Stout, respectively, although the subdivisions are not too dissimilar.

A. Classification by James Ewing

1. *Adult cell liposarcoma:* This tumor is considered to "represent a lawless phase of growth of fat cells observed in lesser degree in chronic inflammation of fat tissue." The neoplastic cells were thought to be derivatives of adult fat cells, resulting in large polyhedral granular cells, spindle cells, and occasional giant cells. The granular cells may or may not contain fat droplets. These liposarcoma cells become diffuse and appear in many grades of anaplasia. The production of mucous tissue and primary growth of blood vessels are not characteristic of the adult cell types of liposarcoma.
2. *Embryonal myxoliposarcoma:* This tumor simulates the embryonal growth of fat tissue. It is associated with a peculiar proliferating capillary vascular system. Between the anastomosing vessels are myxomatous tissue and fetal fat cells.

B. Classification by Arthur Purdy Stout

1. *Well-differentiated myxoid type of liposarcoma:* This tumor resembling embryonal fat is composed of adult fat cells, embryonal stellate cells, or spindle-shaped lipoblasts, with cytoplasmic droplets staining with scharlach R or sudan III. The lipoblasts are usually small, but mitotic figures are seldom seen. These tumors may assume bulky proportions.
2. *Poorly differentiated myxoid type of liposarcoma:* This is a malignant tumor capable of metastasizing and difficult to cure. According to Stout, the characteristic cells are bizarre lipoblasts, sometimes monstrous, containing misshapen pyknotic or hyperchromatic nuclei.
3. *Round cell or adenoid types of liposarcoma:* The tumor cell is spherical with a central nucleus and abundant foamy cytoplasm containing lipoid.

Ewing described two kinds of fat in the adult; common white fat and the less widely distributed brown fat, which he localized as occurring chiefly in the mediastinum, axillae, perirenal region, and about the joints. He described brown fat as opaque, highly colored, a common component of those fatty tumors designated as xanthomatous. Ewing dissected fresh cadavers and amputated limbs in order to study the adipose tissues in the region of the shoulder, knee, hip, and groin to see if information so obtained would shed any light on the origin of lipomatous neoplasms in these locations. Studies of fetal fat, however, were more productive. Ewing found, in the groins and axillae of fetuses, lobulated myxomatous foci amid the so-called brown fat and network of anastomosing blood vessels. He attributed an intimate connection between the capillary vascular network and the growth of fat cells from the mesenchyme. He considered the pattern of blood supply in these fetal fat lobules to be similar to that observed in the embryonal myxoliposarcomas.

Murray and Stout also studied embryonal lipoblasts as a prelude to the consideration of liposarcomas. To quote them, "Fat cells are not just modified fibroblasts but are derived from undifferentiated mesoderm during embryonal life and persist through postnatal life as specialized lipoblasts." They

described the embryonic lipoblasts as being of two types: (a) widely spaced stellate or spindle-shaped cells enveloped by mucoid intercellular substance, and (b) glandlike lobules of rounded or polygonal fat cells of variable size. The cells may contain cytoplasmic droplets of fat.

There are examples wherein one may trace the transformation of a benign myxolipoma to a liposarcoma of low-grade malignancy. The early phase of liposarcoma may be only foci of nuclear hyperchromatism and gigantism found in the midst of apparently normal lipomatous tissue. One should be suspicious if myxomatous foci or the presence of fetallike fat in a lipoma is discovered. Myxolipomas with bluish, mucoid matrix and round vesicular cells of uniform size may be diagnosed as benign, but unfortunately are prone to recur after simple excision, and the recurrent tumors may then be considered malignant.

Murray and Stout have made an important contribution to the accurate determination of the histogenesis of these tumors by employing tissue culture as a diagnostic aid. The liposarcomas seldom appear in pure type; this lack of homogeneity is characteristic of this tumor, which has a remarkable range of variation in histologic structure. Some liposarcomas have almost acellular mucoid pools interspersed in the network of anastomosing blood vessels. The lemon-yellow liposarcomas often contain xanthomatous elements, and may be only moderately malignant. Ewing was of the opinion that the highly pigmented orange-yellow or brown liposarcomas, which are very cellular and quite malignant, contain very little fat and may have originated from brown fat, especially around joints. Ewing also stated that the highly malignant round cell liposarcomas bear a close resemblance to lymphosarcoma. Some liposarcomas also resemble metastatic renal or adrenal tumors to such an extent that erroneous diagnoses occasionally are made. Frozen section and staining with sudan IV will often demonstrate cytoplasmic sudanophilic globules of variable size. The liposarcoma cells are more commonly spindle shaped or oval, with long cytoplasmic processes and long nuclei containing dark granular chromatin and one or more nucleoli. Degenerating, bizarre, and multinucleated giant tumor cells are commonly seen on microscopic study. Sternberg has demonstrated the extension of the sarcomatous cells along the fibrous septa into adjacent normal adipose tissue, and properly offered this as one explanation for local recurrence following conservative removal of these tumors. It may be stated, as a general rule, that the proportion of cytoplasmic fat globules diminishes with the grade of anaplasia.

When the liposarcomas are recurrent or highly malignant, they may be so anaplastic that it is difficult to discover any remnants of the tumor that can be identified as lipoblastic. Pleomorphism is marked. The pathologist may need to consult the primary tumor before he can determine the histogenesis of the recurrent tumor.

The symptomatology and diagnosis of liposarcoma: The malignant lipogenic tumor usually starts as an inconspicuous swelling of the soft tissues, exhibiting progressive steady growth without alarming exacerbation until it

reaches such proportions as to demand the attention of the patient. The patient's chief complaint is the gradual enlargement of a perceptable tumor.

CASE 2. *Incipient or Early Liposarcoma.*—

A 47-year-old woman had been aware for two months of a tiny, slightly painful subcutaneous lump on the ulnar aspect of the left palm. It did not grow in this interval but was a source of constant annoyance because of pain on pressure. There was no history of trauma.

Physical examination was entirely normal except for local findings. There were no enlarged axillary lymph nodes. Situated in the subcutaneous tissues of the left hypothenar eminence was a hard nodule, measuring not greater than 0.5 cm. in diameter. A roentgenogram of the chest was normal.

Under local anesthesia, the lesion was excised and found to be a firm, solid, apparently encapsulated, subcutaneous tumor, measuring not more than 0.25 cm. in diameter. It was yellow in color and appeared to be slightly lobulated. Pathologic diagnosis* was miniature myxoliposarcoma. Postoperative x-ray therapy was given with the following dosage: 500 r through a 2 cm. cone, twice weekly for a total dose of 2,000 r to the operative area, using the following factors: 100 kv., 1 mm. Al filter, 20 cm. target-skin distance. There has been no recurrence after six years.

This tumor is the smallest and earliest liposarcoma discovered in this series.

Pressure symptoms may ensue when the neoplasm reaches a certain size, but pain is quite rare at the onset. The rate of growth of the liposarcomas shows great variability, that is, usually slow, sometimes fast, occasionally quiescent for months or even years, then an exacerbation of growth rate.

On the basis of physical examination alone, certain similarities between adipose deposits, benign lipomas, and liposarcomas have handicapped the early recognition and diagnosis of the more important malignant tumor. As a general rule, liposarcomas are firmer, less easily compressed, and more fixed to underlying tissues, notably fascia, than are their benign counterparts, the lipomas. The first evidence of a deeply situated liposarcoma may be only a uniform swelling of a leg or arm.

Differential diagnosis using x-ray examination with soft tissue technique is helpful but not sufficiently accurate to ensure the benignity of the neoplasm. Deep lipomas appear as translucent lobular masses because simple fat tissue has less density than the enveloping soft tissues; the liposarcomas with more fibrous and myxomatous tissue are relatively more opaque.

Biopsy: Aspiration biopsy has its limitations, but it is a useful adjunct if too much is not expected of it. If the tissue so obtained reveals only normal fat, then the tumor may be a lipoma, or the biopsy may have failed to secure tissue representative of the character of the mass as a whole. Or, the aspiration biopsy may reveal a malignant tumor of undetermined histogenesis, which at least may guide the therapist in his next procedure. Less frequently, the plug of tissue so obtained may enable the pathologist to make the specific diagnosis of liposarcoma. If it is believed that the plan of treatment is dependent on the absolute establishment of a histologic diagnosis, a formal incisional biopsy and frozen section analysis are attempted. The manner in which this

*By Dr. Fred Stewart.

is done depends on the location of the neoplasm and its local status, that is, encapsulated or infiltrative. If it is situated on the extremities and the possibility of an amputation is under consideration, a tourniquet is placed proximal to the lesion while the biopsy is being obtained. If the suspicion of liposarcoma is immediately confirmed and radical local dissection is deemed neither prudent nor feasible, an amputation is carried out above the tourniquet, which has been left in place. If the surgeon finds the tumor to be locally resectable, a formal incisional biopsy is still quite important because the method of local removal varies with the diagnosis, for example, simple enucleation for the benign lipoma and radical dissection for the liposarcoma.

CASE 3. *Palliative Control of Liposarcoma for Twenty Years.*—

A 46-year-old newsdealer was first seen at the Memorial Hospital on April 21, 1933. Four months previously he noticed a small subcutaneous lump near the right elbow. It grew rapidly and was not associated with pain nor did it interfere with function. The patient attributed the trouble to an injury sustained eight months previously when he struck the elbow against the side of a car while throwing papers, although there was no history of ecchymosis.

Physical examination: On the lateral surface of the right arm, just lateral to the antecubital fossa, was a soft-part tumor measuring 6 by 5 cm. It was movable and firm, with a separate inferior nodule (2 cm.) extending from the main tumor. A roentgenogram of the chest was normal. On July 3, 1933, the tumor was dissected under general anesthesia. It was found to lie partially beneath the flexor muscles at the elbow and in the upper arm; it lay on some of the larger nerve ramifications along the brachial artery or its bifurcation. Microscopic study of the specimen led to the diagnosis of spindle cell myxosarcoma, lipogenic.

Postoperative radiation therapy was given to the right epitrochlear region as follows: 1,200 r to each of two portals, anterior and posterior. Factors: 198 kv., 50 cm. target-skin distance, 0.5 Cu filter. Fields: 15.6 by 9 cm. Treatment given between Sept. 18, 1933, and Sept. 20, 1933, inclusive.

Subsequent course: This patient remained well until July 15, 1935, when a recurrent tumor was noted, involving the right cubital region, medial to the scar of the former incision. This recurrence was subcutaneous, movable, and consisted of a spherical mass about 5 cm. in its largest diameter. The patient persistently refused another operation until May 3, 1936. At that time the tumor was found to be five times the size it was at the time of detection and appeared to be adherent to the bone and displaced the vessels in the cubitus. On May 4, 1936, the tumor was again excised. It was found to be intimately attached to the radial nerve, just above the elbow. The mass lay for the most part beneath and between the superior portion of the group of superficial antebrachial flexors, and appeared semisoft and cystic. The distal portion of the biceps and brachialis muscle formed part of the medial boundary superiorly and anteriorly. Anteriorly and laterally the tumor seemed to have a definite capsule; it was easily separated from the surrounding muscles. Following this operation the patient received postoperative x-irradiation to four ports, covering the cubital fossa and the scar for a total of 2,500 r to each portal.

Following this there was no evidence of recurrent sarcoma until July 18, 1938, when a tumor mass, measuring 10 by 8 cm. and situated in the right lateral thigh, was found. On Sept. 19, 1938, it was excised under general anesthesia. On exposure, the tumor was found to lie under the fascia lata but not invading it; it did invade the underlying muscle. It was well encapsulated and measured about 10 by 12 by 6 cm. Pathologic diagnosis of the lesion was spindle and giant cell sarcoma.

The patient did not cooperate in keeping his follow-up appointments. On Aug. 8, 1939, a recurrence, lateral to the scar on the thigh, was found. It was soft, elastic, and measured about 5 cm. in diameter. Also, in the right interscapular region was a hemispherical mass measuring 4 cm. in diameter, representing metastasis. Accordingly, radia-

tion therapy was administered with a 4 Gm. radium element pack giving 8,000 mg. hr. daily at a 10 cm. radium-skin distance for a total of 72,000 mg. hr. to the interscapular tumor and a similar dose to the recurrence in the right thigh. On Sept. 14, 1939, it was noted that there was complete regression of both tumors.

A. *B.*

Fig. 5.—*A*, Liposarcoma of thigh; encapsulated, movable, asymptomatic.
B, Postoperative state, after radical dissection to include removal of muscle groups.

The patient remained in excellent general condition without evidence of recurrent disease, as shown by repeated x-ray films of the chest and physical examinations. On Nov. 27, 1944, he developed an acute respiratory infection which gradually subsided within five to seven days. He noticed, however, severe breathlessness, associated with precordial pains and pain in the left lower chest. X-ray films disclosed no evidence of pulmonary metastasis, but did reveal pericardial effusion. There was no evidence of recurrent liposarcoma in the thigh, elbow, back, or elsewhere. The irregularity of the pericardial shadow and the constant bloody character of the pericardial effusion on each pericardentesis led us to suspect metastatic involvement of the pericardium by the liposarcoma, although no tumor cells were identified in the pericardial fluid. The patient was bedridden, almost moribund, and the cardiac tamponage syndrome was not improving until x-ray therapy was given in fractionated doses over the pericardium. Improvement occurred immediately, and now, eight and one-half years later, the patient is well and asymptomatic.

Comment: The liposarcoma, primary in the cubital fossa, apparently metastasized to soft parts such as thigh, back, and perhaps in the pericardium.

The disease has been well controlled by radiation therapy. This case illustrates well an often-observed course of the disease and a degree of radiosensitivity that is not generally appreciated.

Surgical treatment of liposarcomas: The choice between radical surgical dissection and amputation depends on innumerable factors, such as the degree of malignancy, the regional location, the fixity or mobility, the primary or recurrent status, the presence of regional and distant metastases, and, also important, the experience and judgment of the operator. Some liposarcomas are soft, cellular, anaplastic, and vascular, and sustain the reputation at least of metastasizing with slight trauma. If such a tumor is to be attacked directly by local removal, the dissection should be performed with meticulous gentle care and retraction should always be away from rather than toward the tumor. The soft tissues encompassing the liposarcoma should never be compressed or handled roughly. If the neoplasm is on an extremity and the attempt at local removal fails, either because of technical difficulties or because the surgeon realizes the futility of the effort, an immediate amputation may be performed above the level of the tourniquet.

Fig. 6.—Liposarcoma of buttock, treated by local excision and postoperative irradiation. Fifteen-year definitive cure.

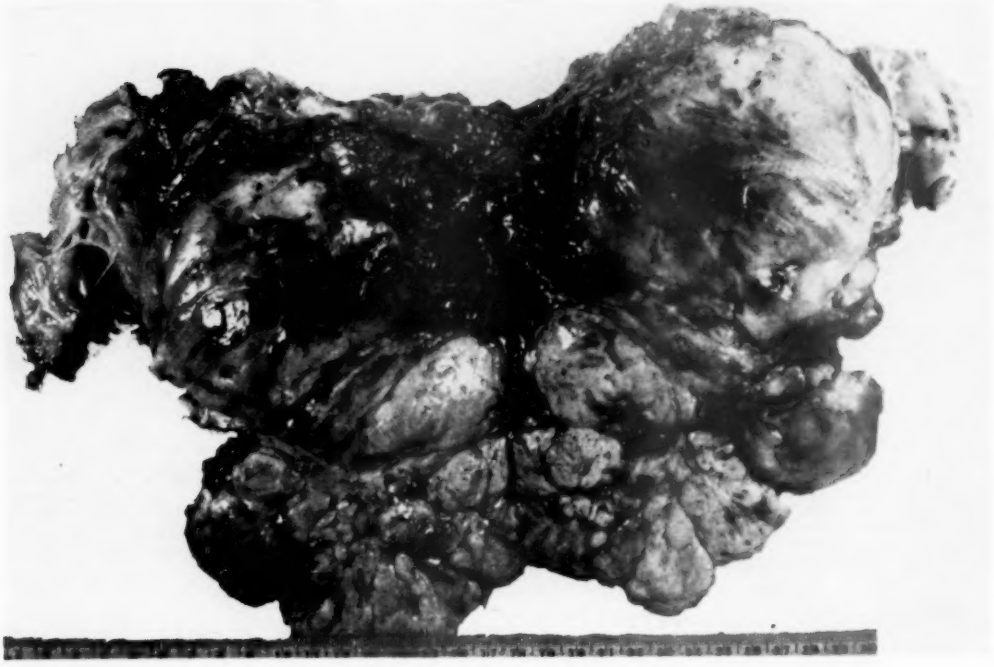
If the region of the liposarcoma has been explored but the lesion is not removed, if a formal incisional biopsy has been carried out, if a previous excision has been followed by recurrent growth of the residual tumor, or if the

fungation of the sarcoma has developed through the wound and the surgeon nevertheless decides that he will attempt a radical dissection, the one imperative technical necessity is that a wide encompassing elliptical excision of skin be made far beyond the limits of the original scar. Not only the scar in the skin but the scarred tract of the incision down to the tumor must be removed in continuity with the sarcoma because of the very real danger of implanted

Fig. 7.—Liposarcoma of femoral region: posttreatment state. The original sarcoma was fungating, fixed, and inoperable, extending into the deeper iliac quadrant. If seen today, it would probably be treated by hemipelvectomy. Original treatment by 4 Gm. radium element pack; 20 cm. radium-skin distance: 8 Gm. hr. daily: total dose, 220,000 mg. hr. Six weeks later surgical dissection and skin graft. Later the patient had medial and lateral Kondoleon operations. Eighteen-year definitive cure.

tumor cells within the previous incision. Recurrent liposarcomas may fungate through the operative scar, become infected and necrotic, and even cause death by sepsis. Some sarcomas grow under tension within their capsule or pseudocapsule, and a break in this barrier may encourage unrestrained growth of the neoplasm along the cleavage plane of the incision.

A.



B.

Fig. 8.—*A*, Gross specimen of liposarcoma, intact specimen. *B*, Cut section, liposarcoma. Characteristic appearance of tumor texture.

Although not always possible of achievement, a good rule to follow is to remove the liposarcoma without seeing or encountering it: by this we mean that the investiture of the neoplasm by muscles, fat, and fascia remains inviolate and that the line of dissection is grossly well beyond the palpable limits of the tumor in all directions. Enucleation of the pseudoencapsulated mass leads to recurrence, with the recurrent tumor more cellular, more anaplastic, and infiltrative rather than expansile in growth. The deeper segments of these liposarcomas are usually more adherent. If the tumor lies above the fascia, then the wide excision should include the fascia. In the compromise of selecting local removal over amputation for these malignant tumors, the surgeon should not relax his vigilance in accepting simple enucleation as an easy substitute for the always essential radical dissection. The entire group of muscles involved by or encompassing the intermuscular liposarcomas should be removed from their origin to their insertions. If the sarcoma is on the extremities, the order of the dissection is from above downward, that is, disengaging the superior limits of the tissue dissection first.

Fig. 9.—Mesenteric and retroperitoneal liposarcoma.

If preoperative irradiation has been given, five or six weeks is permitted to elapse in order for maximal regression to occur and the radiation reaction to subside. Even when the previously palpable liposarcoma has regressed following x-ray therapy so that it is no longer clinically apparent, the wide dis-

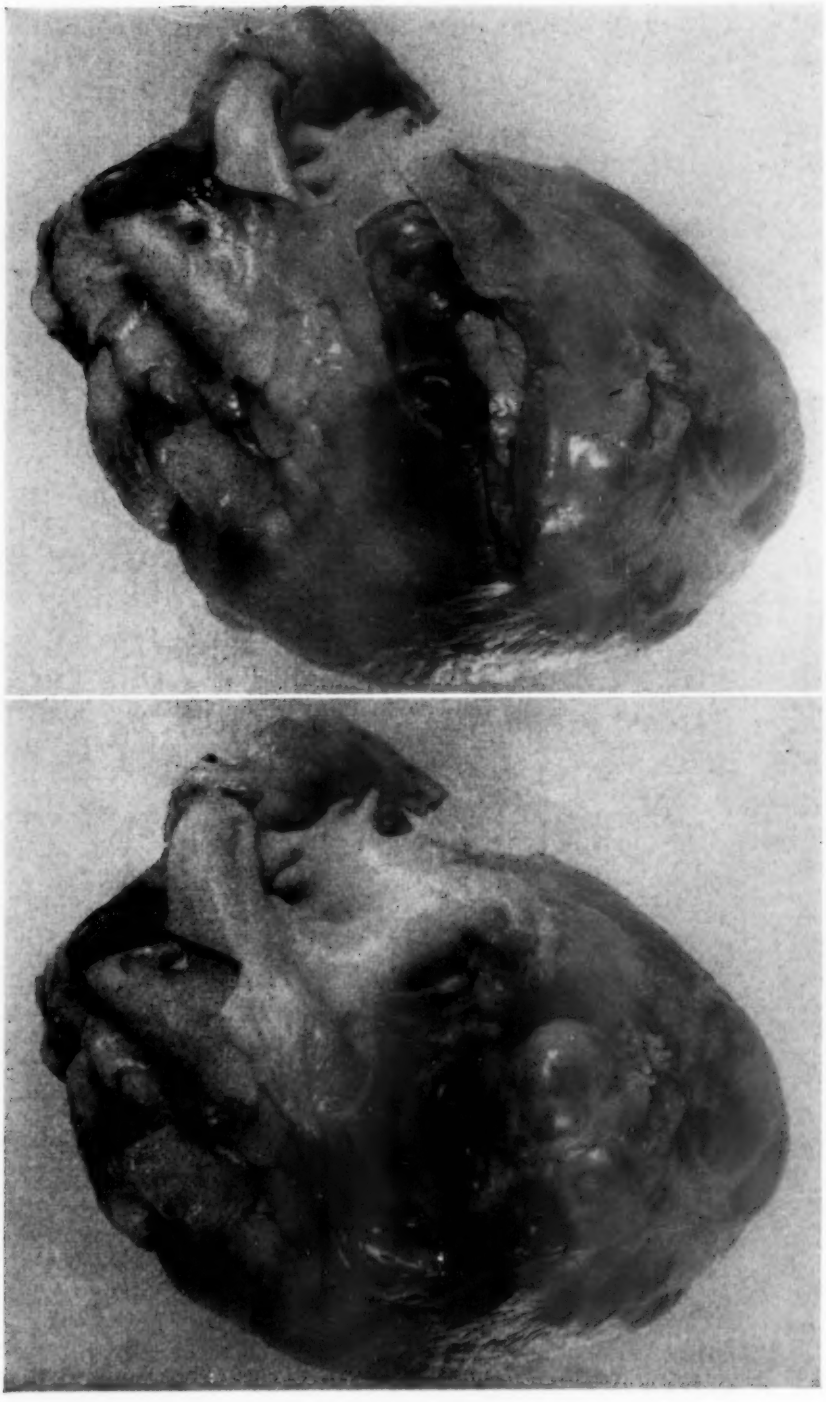


Fig. 10.—Liposarcoma metastatic to heart. Polypoid endocardial metastasis caused valvular obstruction and sudden death.

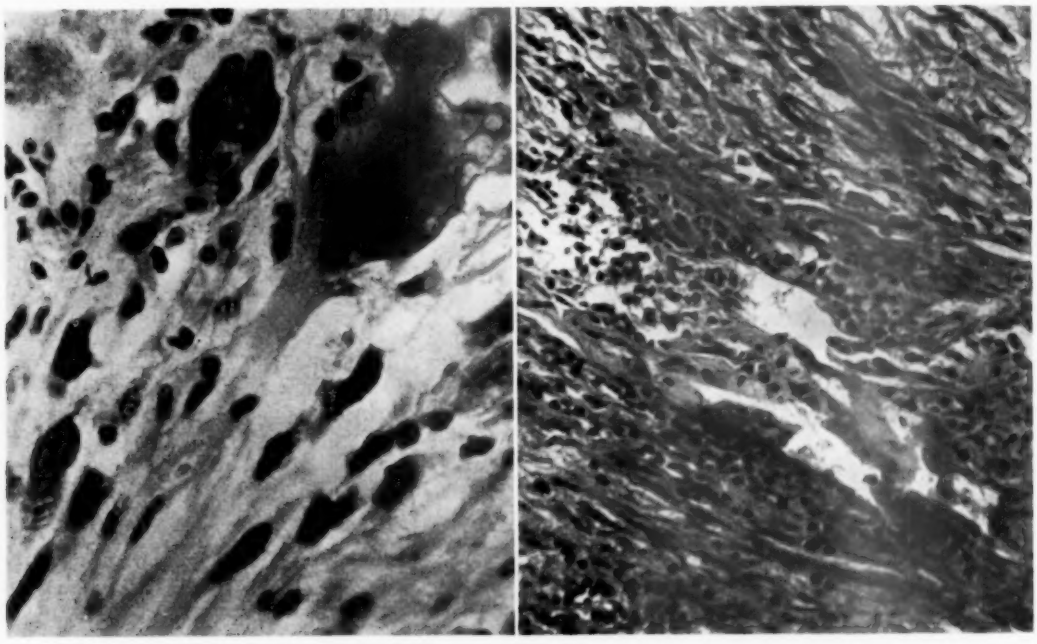
section should still be carried out and the date of operation should not be postponed; residual liposarcoma may be found on microscopic study of the excised specimen.

In the case of amputation for liposarcoma, the upper level of severance must be high if not extreme, sometimes requiring fore- or hindquarter amputations. The general rule of amputating above the level of origin of the muscle groups involved by the sarcoma is a good principle to observe. Amputation may be necessary if there are multiple foci of liposarcoma in the extremity, if the tumor extends indeterminably high along the intermuscular and fascial planes, if it is immovably adherent, especially to important structures, or if it invades bone. Invasion of bone results in subperiosteal and intramedullary extension of the sarcoma superiorly and inferiorly; therefore, amputation through or above the joint with which the affected bone articulates is indicated.

Fig. 11.—Low-power photomicrograph of transected small liposarcoma, predominantly myxomatous.

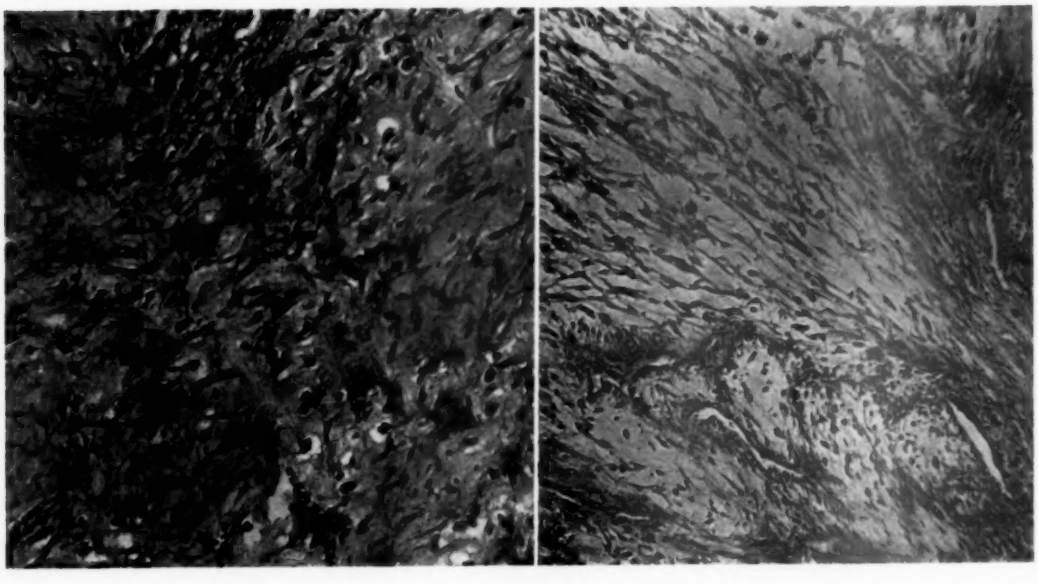
Radiation therapy of liposarcoma: The embryonal myxoliposarcomas are known to be very radiosensitive. This susceptibility in part may be due to the fine capillary blood vessels in the stroma which are easily damaged by irradiation. Recurrent liposarcomas, although more cellular and anaplastic, are sometimes less radiosensitive because their blood supply is obtained from peripheral sources and not from one central vascular system, as Ewing de-

scribed for the primary tumor. It is our opinion that the occasional infection of the recurrent liposarcoma and its invasiveness are the factors more influential in causing these neoplasms to lose their susceptibility to irradiation.



A. *B.*

Fig. 12.—*A*, Bizarre multinucleated giant cells in degenerating liposarcoma. *B*, More cellular liposarcoma with spindle and spheroidal cells.



A. *B.*

Fig. 13.—*A*, Photomicrograph of liposarcoma, showing bluish, mucoid matrix or pools. *B*, Low-power photomicrograph of myxoliposarcoma.

The radiosensitivity of these liposarcomas is greater than their radiocurability; for example, of twelve liposarcomas treated entirely by irradiation, only two (16.6 per cent) were sterilized; one of the patients has enjoyed a cure for more than ten years. During the earlier years of our experience with liposarcomas, preoperative irradiation was routinely employed; subsequent analysis of these cases showed that in 60 per cent of patients a definite regression of

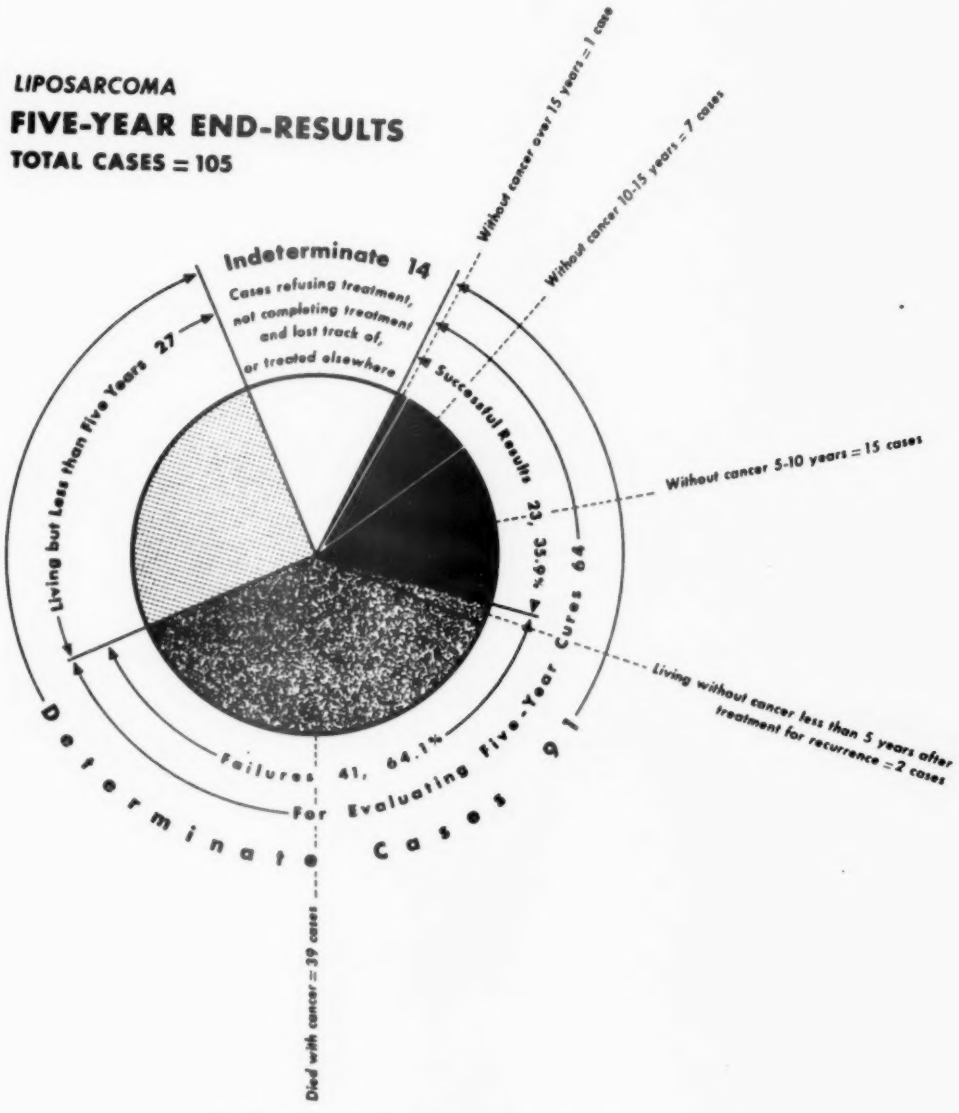

LIPOSARCOMA
FIVE-YEAR END-RESULTS
TOTAL CASES = 105
Indeterminate 14
Cases refusing treatment, not completing treatment and lost track of, or treated elsewhere
Living but Less than Five Years 27
Without cancer over 15 years = 1 case
Without cancer 10-15 years = 7 cases
Successful Results
Without cancer 5-10 years = 15 cases
23, 35.9%
Living without cancer less than 5 years after treatment for recurrence = 2 cases
Failures 41, 64.1%
For Evaluating Five-Year Cures 64
Determinate Cases 91
Died with cancer = 39 cases

Fig. 14.—End results in treatment of liposarcoma.

the tumor occurred, and in 15 per cent of patients the liposarcomas underwent complete clinical disappearance. Microscopic foci of residual sarcoma were found in the majority of surgical specimens subsequently removed. In our group of long-term survivals, all patients but one had received radiation

therapy, usually as an adjunct to surgery. Preoperative irradiation is never employed for liposarcomas overlying bone, for example, scalp, pretibial region, foot, sacrum, and so forth, nor for those invading bone. We have had numerous instances wherein recurrent or primary inoperable liposarcomas have been made technically resectable by preliminary irradiation, for example, in the case of bulky retroperitoneal tumors of this type. We believe that postoperative irradiation is indicated in every instance in which the resected tumor was recurrent. The metastases are usually quite responsive to x-ray therapy, particularly in the frequent cases of multiple subcutaneous spherical deposits which are soft, ecchymotic, and very rapidly growing. One patient with multiple bilateral spherical metastases in the lungs secondary to a liposarcoma of the upper arm received successful palliative x-ray therapy, and is living and well more than ten years postirradiation.

TABLE II. RESPONSE OF LIPOSARCOMAS TO IRRADIATION

	PREOPERATIVE IRRADIATION	POSTOPERATIVE IRRADIATION	IRRADIATION ALONE	TOTAL
1. No regression	1	8	4	13
2. Minimal regression	1	1	1	3
3. Moderate regression	1	2	1	4
4. Good regressoin (50 per cent or more)	1	1	4	6
5. Complete clinical regression	3	2	0	5
6. Sterilization of tumor	0	0	2	2
Total	7	14	12	33

Note: Eleven patients received postoperative radiation therapy as a prophylactic measure, no tumor being clinically detectable when the patient was treated.

End results of treatment of liposarcoma: Of the total cases, primary and recurrent, operable and inoperable, under our care since 1928, 67.7 per cent were suitable for surgical resection, that is, operable; of these, 26.7 per cent were primary operable and 33.3 per cent were recurrent operable. However, in the more recent period from 1944 to 1948, inclusive, the operability rose to 83.3 per cent of all cases, of which 23.3 per cent were primary and 60 per cent were recurrent operable. On the contrary, liposarcomas suitable for palliative treatment, that is, inoperable, decreased from 45 per cent (1928 to 1933) to 16.7 per cent (1944 to 1948). The greatest number of inoperable liposarcomas surprisingly occurred in the thigh; next locations in order of inoperability were those on the chest wall, back, and abdomen (retroperitoneum) (Table III).

Of the 105 total cases of liposarcoma, fourteen were classified as indeterminate or unsuitable for analysis because the patients refused treatment or had their therapy elsewhere. Of the ninety-one determinate cases, twenty-seven patients were treated within the past quinquennial period, leaving sixty-four patients treated more than five years ago (the determinate group). Of these sixty-four patients, two are now living with recurrent sarcoma, thirty-nine are dead of liposarcoma (failures), and twenty-three (35.9 per cent) are living and well (definitive cures). Eight of these patients have been cured for more than ten years (Table IV).

TABLE III. LIPOSARCOMA OPERABILITY ACCORDING TO YEAR OF ADMISSION

TYPE OF CASE	TOTAL CASES		1928-1933		1934-1938		1939-1943		1944-1948	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Total cases	105	100.0	20	100.0	34	100.0	21	100.0	30	100.0
Cases of patients receiving definitive treatment	71	67.6	11	55.0	19	55.9	16	76.2	25	83.3
Primary operable cases	28	26.7	5	25.0	9	26.5	7	33.3	7	23.3
Recurrent operable cases	35	33.3	4	20.0	7	20.6	6	28.6	18	60.0
Cases of patients receiving prophylactic postoperative x-ray therapy (surgery elsewhere)	8	7.6	2	10.0	3	8.8	3	14.3	0	0.0
Cases of patients receiving palliative treatment or none	34	32.4	9	45.0	15	44.1	5	23.8	5	16.7
Primary inoperable cases	9	8.6	1	5.0	5	14.7	1	4.8	2	6.7
Recurrent inoperable cases	19	18.1	7	35.0	8	23.5	2	9.5	2	6.7
Cases of patients refusing treatment	6	5.7	1	5.0	2	5.9	2	9.5	1	3.3

TABLE IV. LIPOSARCOMA: FIVE-YEAR END RESULTS

Total cases					105
Indeterminate cases					14
Cases of patients refusing treatment, not completing treatment, lost track of, or treated elsewhere					
Determinate cases (total to date)				91	
Determinate cases, recent (less than five years)				27	
Determinate cases suitable in time for evaluating five-year cures			64		
Failures: died with liposarcoma			39		
Living without sarcoma under five years after treatment for recurrence			2		
Successful results: without sarcoma five years or more			23		
5-10 years	15	Primary operable cases	12		
10-15 years	7	Recurrent operable cases	4		
Over 15 years	1	Prophylactic x-ray therapy	7		
Five-year cure rate					
Successful results divided by determinate cases		23/64	35.9 per cent		

The end results based on the location of the tumors do not show too great a variability, with the best rates for cure occurring for those liposarcomas of the arm (55 per cent) and foot (50 per cent), and the lowest rates for those on the buttocks (25 per cent) and groin (25 per cent) (Table V).

The end results based on the type of treatment are compared with the over-all curability of 35.9 per cent. Those liposarcomas treated by local excision and postoperative x-ray therapy had a five-year cure rate of 87.5 per cent, because of the very early and favorable stage of their growth. Radical surgical dissection resulted in 66.7 per cent five-year survival without recurrence, which is better than the cure rate following amputation (33.3 per cent), because in past years, amputation has been reserved for the very advanced cases (Tables VI and VII).

TABLE V. LIPOSARCOMA: LOCATION OF TUMOR IN RELATION TO FIVE-YEAR SURVIVAL WITHOUT SARCOMA

LOCATION OF THE TUMOR	CASES AVAILABLE FOR 5-YEAR ANALYSIS			5-YEAR SURVIVALS (PER CENT BASED ON DETERMINATE CASES)		DISTRIBUTION OF DETERMINATE CASES						
						PRIMARY OPERABLE		RECURRENT OPERABLE		PROPHYLACTIC-IRRADIATION		INOPERABLE (NUMBER)
	ALL CASES	INDETERMINATE CASES	DETERMINATE CASES	NUMBER	PER CENT	NUMBER	5-YEAR CURES	NUMBER	5-YEAR CURES	NUMBER	5-YEAR CURES	
All cases	75	11	64	23	35.9	19	12	13	4	8	7	24
Hand	0	0	0	0	0.0	0	0	0	0	0	0	0
Arm	12	3	9	5	55.6	2	2	3	1	2	2	2
Shoulder	6	1	5	2	40.0	2	0	2	2	0	0	1
Foot	2	0	2	1	50.0	0	0	0	0	1	1	1
Leg	5	2	3	1	33.3	0	0	2	0	1	1	0
Thigh	30	3	27	8	29.6	9	5	3	1	3	2	12
Buttock	4	0	4	1	25.0	0	0	1	0	1	1	2
Groin	6	2	4	1	25.0	2	1	0	0	0	0	2
Chest, back, and abdominal wall	10	0	10	4	40.0	4	4	2	0	0	0	4

TABLE VI. TYPE OF TREATMENT OF LIPOSARCOMA IN RELATION TO FIVE-YEAR SURVIVAL WITHOUT SARCOMA BASED ON DETERMINATE CASES AVAILABLE FOR FIVE-YEAR ANALYSIS

TYPE OF TREATMENT	TOTAL CASES			PRIMARY OPERABLE			RECURRENT OPERABLE			INOPERABLE (NUMBER)
		5-YEAR CURES			5-YEAR CURES			5-YEAR CURES		
	TOTAL CASES	NUMBER	PER CENT	TOTAL CASES	NUMBER	PER CENT	TOTAL CASES	NUMBER	PER CENT	
Total cases	64	23	35.9	19	12	63.2	13	4	30.8	24
Excision only	10	5	50.0	5	4	80.0	3	1	33.3	2
Excision and irradiation	15	7	46.7	9	5	55.6	6	2	33.3	0
Amputation	3	1	33.3	0	0	0.0	3	1	33.3	0
Dissection	3	2	66.7	3	2	66.7	0	0	0.0	0
Hip joint disarticulation	1	0	0.0	0	0	0.0	1	0	0.0	0
Prophylactic postoperative irradiation	8	7	87.5	0	0	0.0	0	0	0.0	0
Irradiation only	23	1	4.3	2	1	50.0	0	0	0.0	21
No treatment given	1	0	0.0	0	0	0.0	0	0	0.0	1

TABLE VII. RADICAL SURGICAL TREATMENT OF LIPOSARCOMA

TYPE OF OPERATION	TOTAL CASES	INDETERMINATE CASES	CASES TREATED (PER CENT)	CASES TREATED FIVE YEARS FARLIER	FIVE-YEAR CURES	
					NUMBER	PER CENT
Total cases	14	2	4	8	2	25.0
Amputation	3	–	1	2		
Hip joint disarticulation	3	1	–	2		
Hemipelvectomy	3	–	3	–		
Groin dissection	3	1	–	2	2	100.0
Axillary dissection	2	–	–	2		

REFERENCES

1. Abrams, H. J., and Turberville, J. S.: Liposarcoma of Stomach, South. Surgeon **10:** 891, 1941.
2. Ackerman, L. V., and Wheeler, P.: Liposarcoma, South. M. J. **35:** 156, 1942.
3. Ackerman, L. V.: Multiple Primary Liposarcomas, Am. J. Path. **20:** 789, 1944.
4. Adair, F. E., Pack, G. T., and Farrior, J. H.: Lipomas, Am. J. Cancer **16:** 1104, 1932.
4a. Barnard, W. G.: Review of Article by Stewart, Cancer Rev. **6:** 434, 1931.
5. Beriel, L.: A propos de la classification de certaines tumeurs malignes: les lipomes malins, Lyon chir. **4:** 537, 1910.
6. Beriel, L., and Delachanal, J.: Les tumeurs malignes du tissu cellulo-adipeux (le lipome malin), Arch. de méd. expér. et d'anat. path. **24:** 717, 1912.
7. Blavet di Briga, C.: Trasformazione sarcomatosa di un lipoma mixomatoso, Arch. per le sc. med. **46:** 204, 1923.
8. Case Records of the Massachusetts General Hospital, Liposarcoma of Thigh, New England J. Med. **226:** 204, 1942.
9. Calmann: Ungewöhnlich grosses retroperitoneales Fibro-Lipo-Sarkom, Deutsche med. Wchnschr. **43:** 222, 1917.
10. Delachanal, J.: Des tumeurs malignes du tissu cellulo-adipeux (lipomes malins), 8°, no. 22, Lyon Thesis, 1910, pp. 122.
11. Delachanal, J., and Gayet: Tumeur maligne du cellulo-adipeux (lipome malin), Lyon méd. **117:** 1432, 1911.
12. Ehrmann, W. B.: Ein eigenartiges Angioliposarkom der Niere, Frankfurt. Ztschr. f. Path. **15:** 51, 1914.
13. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, 1928, W. B. Saunders Company, p. 200.
13a. Ewing, J.: Fascial Sarcoma and Intermuscular Myxoliposarcoma, Arch. Surg. **31:** 507, 1935.
14. Fichman, A. M.: Congenital Malignant Tumor of Skin in Newborn, Am. J. Surg. **48:** 456, 1940.
15. Fahr, T., and Lubarsch, O.: Chapter 8, Die Nierengewachse, p. 603: Ortsfremde (heterotope Gewachse), vol. VI, part 1; in Henke, F., and Lubarsch, O. (editors): Handbuch der speziellen pathologischen Anatomie und Histologie. Berlin, 1925, Julius Springer.
16. Froug, C.: Liposarcoma of Kidney; Review of Literature and Case Report, J. Urol. **45:** 290, 1941.
17. Flynn, J. M.: Retroperitoneal Liposarcoma With Myxomatous Degeneration, Radiology **35:** 90, 1940.
18. Garkisch, A.: Retroperitoneales Liposarkom, Beitr. z. klin. Chir. **67:** 61, 1910.
19. Gavrilov, W., and Silberfeld, Y.: Quelques metastases de tumeurs transplantées chez le cobaye (tumeur spontanée de Murray et sarcome provoqué par le radium de Daels), Bull. Assoc. franç. p. l'étude du cancer **27:** 741, 1938.
20. Goormaghtigh, N., Vanderlinden, P., and DePuysseleyr, R.: Lipocytomes et lipocytoses (lipoblastomes et lipoblastoses). Contribution à l'étude des liposarcomes profonds, Cancer, Bruxelles **13:** 3, 1936-1937.
21. Haagensen, C. D., and Krehbiel, O. F.: Liposarcoma Produced by 1:2-Benzpyrene, Am. J. Cancer **27:** 474, 1936.
22. Harbitz, F.: Tuberose Hirnsklerose, gleichzeitig mit Nierengeschwülsten (Myxo-Lipo-Sarkomen) und einer Hautkrankheit (Adenoma sebaceum), Centralbl. f. allg. Path. u. path. Anat. **23:** 868, 1912.
23. Hartwig, C.: Ueber Lipome und Liposarkome der Niere. (Inaugural Diss.) Griefswald, 1903.
24. Havas, L., and Mendeleeff, P.: L'action d'extraits de liposarcome (Murray) et d'extraits d'organes sur la germination et la croissance du blé, Compt. rend. Soc. de biol. **126:** 83, 1937.
25. Hinterberger, H.: Zur Kenntnis des Sarkoma phyllodes lipomatodes mammae, Wien. klin. Wchnschr. **55:** 28, 1942.
26. Jaske, E. A.: Liposarcoma of Mediastinum, M. J. Australia **2:** 236, 1944.
27. Katz, F.: Ueber retroperitoneale Lipome, Beitr. z. klin. Chir. **142:** 864, 1928.
28. Knox, L. C.: Two Cases of Myxo-lipo-sarcoma, Retroperitoneal, Proc. N. York Path. Soc. (New Series) **19:** 90, 1919.
29. Lenger: Lipo-sarcome de la capsule surrénale droite; néphrectomie transpéritonéale; guérison, Ann. Soc. belge de chir. **7:** 128, 1899.
30. Lingley, J. R.: Case Report From Weekly Seminar of Department of Roentgenology, Massachusetts General Hospital, Am. J. Roentgenol. **41:** 851, 1939.
31. McLaughlin, C. W., Jr., and Sharpe, J. C.: Malignant Fatty Tumors of Retroperitoneal Region, Am. J. Surg. **41:** 512, 1938.
32. Mendeleeff, P.: Quelques experiences sur des products de fractionnement du liposarcome de cobaye, Compt. rend. Soc. de biol. **126:** 80, 1937.

33. Mendeleeff, P.: Les variations de l'activité de coeurs isolés et du système musculaire lisse chez les cobayes greffés de liposarcome-murray, Bull. Assoc. franç p. l'étude du cancer **27:** 278, 1938.
34. Menne, F. R., and Birge, R. F.: Primary Liposarcoma of Great Omentum, Arch. Path. **22:** 823, 1936.
35. Moreland, R. B., and McNamara, W. L.: Liposarcoma, Report of 9 Cases, Arch. Surg. **45:** 164, 1942.
36. Murray, M. R., and Stout, A. P.: Characteristics of Liposarcoma Grown in Vitro, Am. J. Path. **19:** 751, 1943.
37. Nienhuis, J. H.: Ein lipoplastisches Sarcom mit Metastasen, Ztschr. f. Krebsforsch. **22:** 434, 1925.
38. Perkins, C. W., and Bowers, R. F.: Liposarcoma of Mediastinum and Lung, Am. J. Roentgenol. **42:** 341, 1939.
39. Schiller, H.: Lipomata in Sarcomatous Transformation, Surg., Gynec. & Obst. **27:** 218, 1918.
40. Shaw, A. F. B.: Embryonal Cell Liposarcoma, J. Path. & Bact. **43:** 277, 1936.
41. Siegmund, H.: Lipoblastische Sarkomatose, Virchows Arch. f. path. Anat. **293:** 458, 1934.
42. Sternberg, S. S.: Liposarcoma Arising Within a Subcutaneous Lipoma, Cancer **5:** 975, 1952.
42a. Stewart, F. W.: Primary Liposarcoma of Bone, Am. J. Path. **7:** 87, 1931.
43. Stout, A. P.: Liposarcoma—Malignant Tumor of Lipoblasts, Ann. Surg. **119:** 86, 1944.
44. Taussig, F. J.: Sarcoma of Vulva, Am. J. Obst. & Gynec. **33:** 1017, 1937.
45. Van Leeuwen, G. A.: Over een zeer groot retroperitoneal gelegen cysto-myo-lipo-sarco-fibroma, Nederl. Tijdschr. v. Geneesk. **51:** 434, 1915.
46. Virchow, R.: Ein Fall von bösartigen, zum Theil in der Form des Neuroms auftretenden Fettgeschwülsten, Virchows Arch. f. path. Anat. **11:** 281, 1857.
47. Waldeyer, W.: Grosses Lipo-Myxom des Mesenteriums mit secondaren sarcomatosen Heerden in der Leber und Lunge, Virchows Arch. f. path. Anat. **32:** 543, 1865.
48. Williams, C.: Retroperitoneal Lipomyxosarcoma, J. A. M. A. **105:** 195, 1935.
49. Wohlgemuth, H.: Demonstration eines Myxosarkoms aus einem Lipom enstanden, Verhandl. d. Berl. med. Gesellsch. **40:** 22, 1910.
50. Wright, C. J. E.: Liposarcoma Arising in a Single Lipoma, J. Path. & Bact. **60:** 483, 1948.
51. Zappoli, A.: Liposarcoma, Bull. d. sc. med., Bologna (third series) **3:** 5, 1843.

ADAMANTINOMA OF THE MANDIBLE: ANALYSIS OF SURGICAL TREATMENT

ROBIN M. RANKOW, M.D., AND MAURICE J. HICKEY, M.D., NEW YORK, N. Y.

(From the Department of Surgery, College of Physicians and Surgeons, Columbia University, and the Surgical Service of the Presbyterian Hospital)

THE adamantinoma or adamantoblastoma is an epithelial tumor with an enamel-forming potential arising from the embryonal odontogenic tissues. It has been most commonly reported in the mandible and, on occasion, in the maxilla. Rarely, tissues resembling the adamantinoma have been described in the tibia and the hypophysis of the pituitary.

This tumor was first described by Broca[1] in 1868. In 1931, McFarland and Patterson[2] reviewed the literature and collected 196 cases of adamantinoma of the jaws. Numerous writers, including Kegel,[3] Lubitsch,[4] Havens,[5] Chin,[6] Thoma,[7] and Zegarelli,[8] have made special studies of the histologic characteristics of these tumors. Robinson,[9] in 1937, documented 379 cases and carefully outlined the statistical findings from these reports.

However, there has never been unanimity of opinion concerning the pathologic characteristics of this tumor. In general, it has been felt that the adamantinoma is histologically a benign lesion with a distinct tendency to recur locally. Most of the writers on this subject have preferred to consider them persistent, expansive, benign growths with a poor prognosis. The relatively few malignant cases reported have been considered atypical. Descriptions of metastases have never been completely acceptable. Stout[10] has maintained that for practical purposes the probability that any given adamantinoma might metastasize is quite negligible.

Still, there has been an increasing trend toward radical resection of the mandible in an effort to remove the tumor en bloc, as outlined by Simmons,[11] Brown,[12] Ivy and Curtis,[13] and Byars and Sarnat.[14] This has minimized recurrences, but there remains a fundamental sphere of controversy as to whether recurrences of the adamantinoma have been due to ineffective, local surgical treatment or to a multicentric potentiality.

Accordingly, the proponents of resection have suggested that the lesion initially, or after the first inadequate curettement, possesses inaccessible, microscopic, fingerlike extensions of the tumor cells into the adjacent bony lacunae or crypts. These may have been present initially, or may have followed the curettement of a fibrous periphery with a spillage of tumor cells into exposed raw bone.

Conversely, the presence of a true infiltration and invasion of bone by the adamantinoma has been questioned. It is suggested that the growth of the tumor is the result of the proliferation of the tumor epithelium into daughter

Received for publication, Jan. 13, 1954.

cysts and lobes within an intact fibrous periphery which, in turn, expand and erode the adjacent bone. Also, the adamantinoma may be transformed from a solid to a cystic form by degeneration of the stellate reticulum-like cells. In the early solid stage, curettements may have been adequate. When transition to the cystic form occurs, strands of adamantoblastic tissue may infiltrate the bony spaces so that local curettement could not suffice.

During the thirty-year interval from 1921 to 1950 inclusive, there have been twenty-nine Presbyterian Hospital admissions with established histopathologic diagnosis of adamantinoma of the mandible. In view of the questioned accuracy of the disease in the maxilla, tibia, and hypophysis, it has been elected to restrict this discussion to adamantinoma of the mandible.

CASE REPORTS

CASE 1.—(P.H. 64248) W. F., an 8-year-old white boy, was admitted to the Presbyterian Hospital on Nov. 4, 1925, with a seven weeks' history of a painless swelling of the right side of the face. Physical examination revealed a firm, adherent mandibular swelling about the size of a "pigeon's egg." The teeth were negative, as was the remainder of the physical examination. A preoperative diagnosis of adamantinoma was made on the basis of clinical and x-ray findings.

On Nov. 6, 1925, an incision was made over the alveolar border, and the soft tissues were retracted. The cystic wall was ronguered, and the contents were curetted to a clean bony cavity. The defect was packed with iodoform gauze after the mucosal flap was invaginated into the cystic cavity. After an immediate period of pyrexia, the postoperative course was relatively uneventful. Histologic examination of the tumor tissue described an adamantinoma of the mandible.

In January, 1927, the mandible was healed without deformity. At the last surgical follow-up by letter on Feb. 13, 1945, the patient was still free from any difficulty with the jaws, after more than twenty-three years.

CASE 2.—(P.H. 611866) E. R., a 68-year-old widowed white woman, entered the Presbyterian Hospital with a recurrent swelling of the left mandible of ten months' duration. She had had all her teeth removed eighteen years prior to admission. A tumor mass appeared in the left molar area six years after these extractions. The bone was "scraped," and healing followed. However, five years later the mass recurred. There was no pain at this time of admission.

The physical examination was negative except for moderate obesity and bilateral, early senile cataracts. The mouth was edentulous. On the margin of the left mandible an irregular, marble-sized, bony mass was evident. A biopsy led to a report of adamantinoma. On June 10, 1940, an intraoral, partial ostectomy was performed including enucleation and curettement of the bony defect.

The patient did well postoperatively. At the last surgical follow-up, in March, 1952, there was no evidence of recurrence twelve years after the local ostectomy.

CASE 3.—(P.H. 809511) H. M. W., a 28-year-old Negro housewife, was admitted in January, 1934, to the Presbyterian Hospital for an intraoral growth on the lower right angle of the mandible of two years' duration. The patient had a "last" right molar extracted in June, 1929. Severe, constant pain and occasional hemorrhage ensued. X-ray films revealed an unerupted wisdom tooth in the operative area. This was extracted, and dressings of the wound were inserted repeatedly for about one year. The patient remained asymptomatic for three years, when a constant, radiating pain from jaw to ear and neck was present. Except for a six-month attack of malaria in 1920, the past history was noncontributory.

On physical examination a firm, odorless, tender, craterlike, red swelling was present in the mouth over the right molar area.

At operation on Feb. 27, 1934, the tumor mass was removed in fragments, and an intraoral, partial ostectomy was performed. A Thiersch graft from the right thigh for an epithelial inlay was also inserted. Histologic report of the tissue described an adamantinoma eroding and advancing in bone in the decalcified sections, although confined in a dense collagenous capsule.

One year after this operation, the tumor had recurred in the adjacent soft tissues over the masseter and internal pterygoid muscles as well as the tonsillar fauces. The tumor mass gradually encroached onto the right pharyngeal region and impinged against the maxilla. On May 21, 1940, a hemiresection of the mandible was performed. Histologic examination of the specimen indicated a complete excision. The postoperative course was complicated by the appearance of a buccal fistula on the tenth day. This closed spontaneously after a two-week interval.

The patient was last seen in surgical follow-up clinic in October, 1952. She was free from disease more than twelve years following the hemiresection of the mandible.

CASE 4.—(P.H. 666223) F. B., a 30-year-old Negro man, was admitted to the Hospital on March 21, 1930, with a recurrent swelling of the right mandible of fifteen years' duration. Since 1915 the patient had this painless growth, which required repeated incisions for drainage. At the fourth such treatment, in 1916, an unerupted right wisdom tooth was removed followed by prolonged chronic sequestration, culminating in a pathologic fracture in 1928. In 1930 another tooth was removed, and a tissue diagnosis of adamantinoma was made.

On physical examination a projecting, 9 by 7 cm., hard, facial swelling was present at the angle of the right lower jaw. There were two, healed, extraoral scars. A discharging, purplish, intraoral mass corresponding to the facial swelling was present over the right posterior portion of the mandible. The Wassermann test was 4 plus. Other physical findings of interest were arteriosclerosis and a hypertrophied prostate.

A biopsy specimen was taken and reported as an adamantinoma.

From April to July, 1930, a course of extraoral radiotherapy was given. The mass was markedly reduced, and the discharge curtailed to a small amount from a central, necrotic portion. However, another recurrence was evident in March, 1932. The microscopic report at that time was similar to the report of the previous section. There were also early squamous epithelium changes following radiation. Accordingly, on April 26, 1932, a right hemiresection of the mandible was performed. The specimen revealed an unerupted tooth in the right angle of the mandible. The tumor appeared adequately excised, and no microscopic evidence of bony invasion was present.

The postoperative course was uneventful. The patient was discharged home on the twelfth postoperative day. The patient has remained free from disease, and last reported by letter on Feb. 21, 1952, twenty years following the hemiresection.

CASE 5.—(P.H. 875628) R. M., a 50-year-old white man, was admitted to the Hospital in September, 1947, for a left, recurrent swelling of the mandible of three years' duration. In 1944 a diagnosis of adamantinoma was made from a biopsy taken in the outpatient dental clinic. After several local curettages and small recurrences, the patient noted a rapid increase in size in the eight months preceding admission. A dull, persistent ache was present in the lower right jaw during the three to four weeks previous to admission.

On Sept. 11, 1947, a left hemiresection of the mandible including the condyle and muscle attachments was performed. The internal pterygoid muscle was invaded by the tumor, but an adequate margin of excision was present.

The postoperative course was uneventful. The patient was discharged home on the twelfth postoperative day. He has been followed regularly, and when last seen on March 25, 1953, was free from any evidence of disease, six years following hemiresection.

CASE 6.—(P.H. 495119) T. R., a 24-year-old Negro, was admitted to the Presbyterian Hospital on Aug. 18, 1936, for a recurrent growth on the left mandible. In 1924 the patient

had a circumscribed, pea-sized, nontender nodule on the left mandible which had ruptured spontaneously into the oral cavity. Again, in 1926, the patient had an undetermined facial operation over this site. Two years prior to the 1936 admission the swelling recurred, associated with a dull, throbbing pain.

Physical examination revealed a 2 by 2 by 0.5 cm., smooth, firm, intraoral mass partially adherent to the outer surface of the left ramus of the mandible. There was a healed, 7 cm. linear facial scar over the left angle of the mandible.

On Aug. 19, 1936, an intraoral, partial resection of the mandible with excision and curettement of the tumor was performed. The histologic report from decalcified sections indicated an invasion of adjacent bone by the adamantinoma.

Twenty-one months later, a stony hard mass extending from the left angle of the mandible to the zygoma had appeared. There was persistent soreness in the region of the temporomandibular joint. The patient was readmitted to the Hospital, and on Dec. 14, 1938, a left hemiresection of the mandible was performed. There was an inadvertent rupture of the cystic cavity and partial section of the mandibular and zygomatic branches of the facial nerve at the time of operation. The facial nerve soon resumed its normal function in the course of an uneventful postoperative period. There was a question of an adequate margin of excision at the incisor area, but all of the tumor had been removed.

The patient has been seen periodically in the surgical follow-up clinic. The last visit was in October, 1952, at which time the patient was completely free from disease, sixteen years following the hemiresection of the mandible.

CASE 7.—(P.H. 587951) J. B., a 24-year-old Negro man, was admitted to the Hospital on Aug. 21, 1929, for a growth on the mandible of nine years' duration. At that time, the patient had a left lower molar removed. A painless, recurrent swelling soon appeared. This was incised and drained but reappeared shortly thereafter. A firm fullness of the left jaw was evident. Intraorally, there was a swelling in the mouth over the left ramus of the mandible extending from the retromolar tissues.

On Aug. 26, 1929, a local excision and curettage of the oral lesion were performed. The histologic report was that of a paradental epithelial cyst of the mandible.

The mass again recurred, and on May 17, 1935, an intraoral excision was performed. There was microscopic evidence of islands of adamantinoma growing into the bone marrow.

Recurrence was definitely present once again in January, 1939. Finally, a left hemiresection of the mandible was performed on Aug. 15, 1939. A review of the original slides* stated that the original diagnosis of paradental epithelial cyst was in error, and that the lesion was an adamantinoma from the beginning.

The patient did well in the immediate postoperative period. He has been seen subsequently on visits to the surgical follow-up clinic. On April 10, 1952, the patient was free from any evidence of recurrence of the disease, twelve years following hemiresection of the mandible.

CASE 8.—(P.H. 498448) J. W., a 38-year-old white housewife, was admitted to the Hospital on Sept. 16, 1936, with a recurrent, painless swelling of the left portion of the mandible following an extraction of a tooth twelve years previously. Previous recurrences had been locally excised in 1934, 1935, and again in May, 1936, when the microscopic diagnosis of adamantinoma was established.

The general physical examination of this short, very obese woman was essentially noncontributory except for a blood pressure of 142/92. The tonsils were hypertrophied. The teeth were in fair condition. In the midmandibular region on the left there was a hard, smooth swelling of the buccal bone. The dental ridge was enlarged, and over the molar area a purplish discoloration was present.

On Sept. 28, 1936, a left hemiresection of the mandible was performed.

*By Dr. A. P. Stout and Dr. V. K. Frantz of the surgical pathology laboratory.

The postoperative course was uneventful. The patient was discharged home on the thirteenth postoperative day. At the last follow-up visit in September, 1952, the patient had remained free from disease sixteen years following hemiresection of the mandible.

CASE 9.—(P.H. 931291) F. M., a 56-year-old white man, was admitted to the Hospital on Nov. 15, 1948, with a painless, slow-growing adamantinoma of the right portion of the mandible of seventeen years' duration. The tumor mass had been drained several times prior to admission, but recurred repeatedly.

The general physical examination revealed a chronic pulmonary emphysema and a mild hypertension. Radiographic and clinical examination of the region of the right angle of the mandible indicated a large mass which had extended up the ramus toward the glenoid fossa. It bulged laterally under the zygomatic arch and forward into the temporal muscle.

On Nov. 16, 1948, a right hemiresection of the mandible was performed. Microscopically, the excision appeared adequate.

The postoperative course was uneventful. The patient was discharged home on the eighth postoperative day. At the last follow-up examination in March, 1953, there was good mandibular function, and the patient was still free from recurrence five years following the hemiresection of the mandible.

COMMENT

The clinical data for this disease have often been presented and require only a brief elaboration in this paper. It is noted, however, that in this series of twenty-nine patients, the average age was 30 years, with a range of from 4 to 72 years. There were seventeen female and twelve male patients. The race distribution was eighteen white and ten Negro patients and one patient of the Mongolian race.

In the cases at this hospital, twenty-two of the twenty-nine patients had a history of an involved tooth or dentigerous cyst coincidentally present with the tumor lesion. This may be in accord with the experimental impression by Zegarelli that "dentigerous, follicular and multilocular cysts are stages of adamantinomas and comparable to the pure monocystic and multicystic stages."

Similarly, in this group of patients, the recurrences following local and radical treatments of adamantinoma of the mandible are outlined in Table I. These recurrences have appeared within an average of three years, ranging from intervals of a few months to ten years.

It is of interest that the two cures following local treatment occurred in children aged 4 and 8 years, respectively. It is possible that a low growth potential or ready accessibility of an early tumor to local excision may be related to these cures.

In this small group, there was one cure (Case 2) which was characterized histologically by a very small amount of adamantoblastic tissue. This tissue was well encompassed within an intact fibrous tissue, which may explain the success of the excision. One recurrence in this group was felt to be a probable adenocarcinoma rather than an adamantinoma. This patient had several recurrences, and ultimately died from inanition. The other recurrence (Case 3) was finally treated by hemiresection. The original specimen showed microscopic evidence of tumor eroding and advancing in bone in the decalcified sections. Massive recurrence occurred within one year following this intraoral

ostectomy. At this time, even muscle was invaded by tumor, but an adequate margin of excision in the hemiresection was present.

TABLE I. RECURRENCES FOLLOWING LOCAL AND RADICAL TREATMENT OF ADAMANTINOMA OF MANDIBLE (PRESBYTERIAN HOSPITAL, 1921-1950)

Total patients admitted		29
Lost to follow-up		6
Refused treatment (after biopsy)		1
Local Treatment in 22 Patients		
Cures—	2	9%
1 Excision of cyst (more than 10 yr.)		
1 Local curettage and radium (more than 10 yr.)		
Recurrences—	20	91%
Radical Treatment in 20 Patients		
I. (a) Intraoral partial ostectomies		2
1 Cure (more than 10 yr.)		
1 Recurrence (subsequent hemiresection)		
(b) Intraoral partial ostectomy plus radium		1
0 Cures		
1 Recurrence (not resectable ? carcinoma)		
II. Hemiresections		18
18 Cures*		
0 Recurrences		

*12 cures more than 10 yr.
4 cures more than 5 yr.
2 cures more than 3 yr.

There have been eighteen hemiresections, which include seventeen recurrences following repeated local curettages and one recurrence following intraoral partial ostectomy, as noted previously.

Although it is too soon to judge the final outcome of therapy in a disease characterized by long remissions, there have been no recurrences to date in the eighteen hemiresections. Twelve of these patients have been free from disease more than ten years. Four of the remaining six patients have been more than five years without recurrence, and the other two patients have had no further difficulty for three years.

SUMMARY

Twenty-nine cases of patients with adamantinoma of the mandible admitted to the Presbyterian Hospital during the past thirty years are reviewed.

An incidence of 91 per cent recurrence has followed local curettement measures in the management of these adamantinomas. By contrast, there have been no recurrences to date following eighteen hemiresections of the mandible.

REFERENCES

1. Broca, P.: Gaz. hebd. d. sc. méd. de Bordeaux **25**: 70, 1868.
2. McFarland, J., and Patterson, H. M.: Adamantinomata, D. Cosmos **73**: 656, 1931.
3. Kegel, R. F. C.: Central Tumors of the Lower Jaw, Radiology **16**: 216, 1931.
4. Lubitsch, K.: Adamantinoma of the Jaw, Acta radiol. **26**: 441, 1945.
5. Havens, F. Z.: Adamantinoma of the Jaw, Arch. Clin. Oral Path. **4**: 284, 1940.
6. Chin, K. Y.: Adamantinoma: Pathological Study of Forty-One Cases, Chinese M. J. (supp.) p. 91 (March), 1938.
7. Thoma, K.: Clinical Pathology of the Jaws, Springfield, 1934, Charles C Thomas, Publisher, pp. 394-429.

8. Zegarelli, E.: Adamantoblastomas in the Slye Stock of Mice, Am. J. Path. **20:** 23, 1944.
9. Robinson, H. B. G.: Ameloblastoma—Survey of 379 Cases From the Literature, Arch. Path. **23:** 831, 1937.
10. Stout, A. P.: Human Cancer, Philadelphia, 1932, Lea & Febiger, pp. 54-64.
11. Simmons, C. C.: Adamantinoma, Ann. Surg. **88:** 693, 1928.
12. Brown, J. B.: Cystic Adamantinoma With Resection, Including the Condyle, From the Inside of the Mouth, Internat. J. Orthodontia **18:** 1104, 1932.
13. Ivy, R. H., and Curtis, L.: Adamantinoma of the Jaw, Ann. Surg. **105:** 125, 1937.
14. Byars, L. T., and Sarnat, B. G.: Surgery of the Mandible. The Ameloblastoma, Surg., Gynec. & Obst. **81:** 575, 1945.
15. Stout, A. P., and Frantz, V. K.: Personal communication.

WILL FAT EMULSIONS GIVEN INTRAVENOUSLY PROMOTE PROTEIN SYNTHESIS? METABOLIC STUDIES ON NORMAL SUBJECTS AND SURGICAL PATIENTS*

THEODORE B. VAN ITALLIE, M.D.,** FRANCIS D. MOORE, M.D.,
ROBERT P. GEYER, PH.D., AND FREDRICK J. STARE, M.D.,
BOSTON, MASS.

(From the Department of Nutrition, Harvard School of Public Health, the Department of Surgery, Harvard Medical School, and the Surgical Service, Peter Bent Brigham Hospital)

UTILIZATION of fat emulsions administered intravenously has been demonstrated in animals by means of a variety of techniques. For example, experiments have shown that the respiratory quotient may display a significant drop after fat has been given intravenously.[1] Fat emulsions given by vein can maintain weight and nitrogen equilibrium in mature dogs receiving an oral diet inadequate in calories.[2] It has been found that puppies receiving up to 30 per cent of their total energy requirements from fat emulsions given by vein grow as well as control animals receiving the same amount of fat in the diet.[3] Last, C^{14}-labeled fat in a finely emulsified form has been shown to be rapidly and extensively metabolized in the rat when it is given intravenously.[4, 5]

Prolonged studies on the metabolic effects of intravenous fat in man have been restricted because of the difficulties inherent in obtaining consistently nonpyrogenic and uniformly stable fat preparations.[6] One brief clinical study has been reported in which the use of emulsified coconut oil given by vein as a source of calories supplementary to a calorically inadequate diet was associated with a diminution in nitrogen and potassium excretion.[7] More recently, it has been shown that the intravenous administration of fat emulsions to man may be associated with a variable rise in blood ketones.[8] This has been interpreted as further evidence of utilization of the emulsified lipids given intravenously.

In this report, studies on the metabolic effects of fat emulsions administered intravenously to two healthy volunteer subjects and to two surgical patients are described.

PROCEDURE AND RESULTS

Materials.—The fat emulsions used in these experiments had the following composition per 100 ml.; vegetable oil 15 Gm., phosphatide preparation† 1 Gm., Demal-14‡ 1 Gm., dextrose 4.3 Gm. In Experiment 1, the vegetable oil com-

Received for publication Feb. 23, 1954.

*Supported in part by grants-in-aid from the Nutrition Foundation, Inc., New York; The Upjohn Company, Kalamazoo, Michigan; Armour & Company, Chicago; Atlas Powder Company, Wilmington, Delaware; Winthrop-Stearns, Inc., New York; the Atomic Energy Commission; and under contract with the Research and Development Board, Surgeon General of the Army.

**Present address: Department of Medicine, St. Luke's Hospital, New York.

†Prepared from Glidden Grade "RG" Soybean Lecithin obtained from the Glidden Company, Chicago.

‡Kindly furnished by the Emulsol Corporation, Chicago.

ponent consisted of equal parts of coconut oil and olive oil; in Experiment 2, olive oil alone was used; in Experiments 3 and 4, coconut oil was used.

All the lipid materials were filtered through bacteria-retaining filters before use. Emulsification was accomplished by means of a Manton-Gaulin* Model 125-E homogenizer fitted with special stainless steel auxiliary equipment. Preparation of the emulsion was carried out under nitrogen, and the finished product was autoclaved at 15 pounds per square inch in sealed bottles. Storage was at 5° C. in the dark.

Each batch of emulsion was tested in rabbits for pyrogenicity,† and in rats and dogs for toxicity. Samples from each batch of emulsion were cultured on a variety of media in order to ascertain their sterility.

Methods of Analysis.—Representative portions of diets were homogenized and analyzed for their content of nitrogen, potassium, and sodium. Feces were prepared similarly and analyzed. Urinary potassium, sodium, and nitrogen were measured directly. All determinations were made in duplicate on aliquot samples.

Total nitrogen was determined by a macro-Kjeldahl method. Potassium and sodium were determined by means of a flame photometer, the fecal and dietary aliquot samples having been first ashed and extracted and made up to volume with hydrochloric acid.

Eosinophil counts were taken by the method of Dunger.[9] Caloric intake was calculated from weighed portions and refusals on the basis of standard tables.[10]

I. *Normal Subjects.*—

Experiment 1. Constant marginal protein intake: A volunteer male subject, M. M. (aged 21 years, weight 66 kilograms, height 182 cm.), was studied in the hospital. He remained ambulatory but at light activity during the course of the experimental period. He was healthy and gave no history of recent illness.

The experiment was divided into three parts:

Period I comprised seven days during which the diet supplied a daily allowance of 947 calories and 7.8 Gm. of nitrogen (49 Gm. of protein). The approximate daily intakes of potassium and sodium were 58 meq. and 100 meq., respectively. Day-by-day oral intake remained virtually constant throughout the entire study period. Prior to admission to the hospital, the subject had voluntarily restricted nitrogen intake at home to 4.0 Gm. per day for four days.

Period II lasted five days, and the oral intake was essentially the same as that in Period I. Intravenous fat emulsion was given as a caloric supplement during this time. The extra calories derived from the fat in the intravenous fat emulsions during this period totaled 4,640 and averaged 930 calories per day. Carbohydrate in the oral diet was reduced by approximately the amount provided by the fat emulsion.

Period III lasted five days and was identical to Period I with respect to intake.

*Manton-Gaulin Co., Everett, Massachusetts.

†No pyrogenic reactions were observed in the four subjects who participated in the experiments.

Results in Experiment 1 (Table I and Fig. 1): The subject's seven days of calorie and nitrogen restriction during Period I were associated with a persistently negative nitrogen balance which averaged −3.36 ± 0.75 Gm.* per day. Levels of circulating eosinophils fell as the period of fasting progressed. The potassium balance was negative during the first period, averaging −14.19 ± 5.58 meq. per day. The K:N deficit ratio (milliequivalents of potassium to

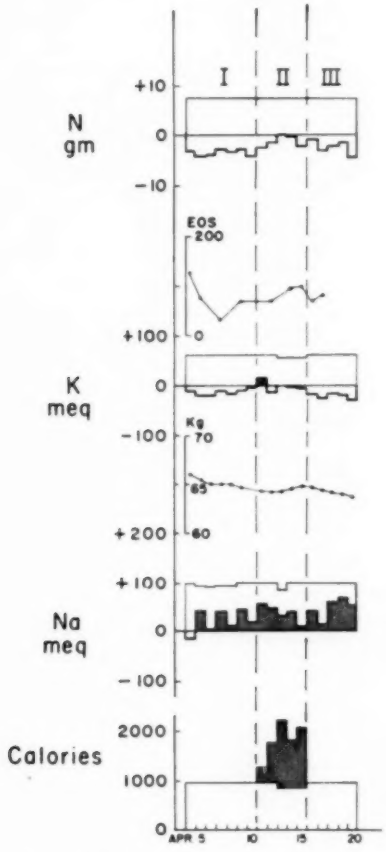


Fig. 1.—Decrease in nitrogen and potassium deficits following intravenous fat administration in a normal subject on a low calorie, marginal nitrogen intake. Experiment 1.
Nitrogen, potassium, and sodium intakes are charted upward from the 0 line, and outputs are charted downward from the top of the intake line. An excess of output over intake is seen as an area below the 0 line: if output is less than intake, the difference is represented by a shaded area above the 0 line. Horizontally lined areas designate caloric contribution of intravenous fat emulsion.

grams of nitrogen) for this period was approximately 4.2:1. The subject's weight fell steadily from 66.0 kilograms to 64.2 kilograms (average per day −0.26 kilogram). The sodium balance during Period I was positive and totaled 160.9 meq. (average per day + 23 meq.).

During Period II while the intravenous fat was being administered, certain definite changes in metabolic trend were noted. The nitrogen deficit diminished considerably, averaging only −1.16 ± 1.09 Gm. per day. Eosinophil values rose

*Standard deviation of individual values around the mean. (s.d. = $\sqrt{\frac{\Sigma (X - X_i)}{n - 1}}$.)

somewhat as Period II progressed, and potassium balance reached virtual equilibrium, averaging −2.08 ± 11.66 meq. per day. The negative weight trend was arrested, and the subject actually displayed a gain in weight of 0.4 kilogram. The sodium balance during Period II totaled + 200 meq.

During the third period, after intravenous fat had been discontinued, the subject's nitrogen deficit again increased appreciably. The nitrogen balance on the first day of Period III was only −0.6 Gm.; however, the total deficit for the five days was 11.2 Gm., with the negative balance averaging −2.24 ± 1.48 Gm. per day. Eosinophils again showed a downward trend. The potassium balance became much more negative, averaging −22.26 ± 6.31 meq. per day, and weight loss again occurred (−1.0 kilogram). The sodium balance during Period III totaled +240 meq.

A statistical comparison of the mean nitrogen and potassium balances for the control and experimental periods is presented in Table I.

Experiment 2. Constant inadequate protein intake: A second normal male subject, J. B. (aged 26 years, weight 74.6 kilograms, height 176.5 cm.), also was studied in the hospital. His activity remained light during the experiment. He, too, had always been in good health.

The experiment was divided into two periods:

Period I comprised four days during which the diet supplied a daily allowance of approximately 1,500 calories and 3.0 Gm. of nitrogen (18.8 Gm. of protein). The approximate daily intakes of potassium and sodium were 50 meq. and 77 meq., respectively. The day-by-day oral intake remained virtually constant throughout the entire experiment; however, during Period I the oral diet was supplemented by daily infusions of intravenous fat emulsion. Four such infusions were given and added a total of 4,800 calories to the intake during Period I (average 1,200 calories per day). For four days prior to the beginning of the experiment the subject had been on a preparatory diet which limited him to 3.0 Gm. of nitrogen per day. On the last day of the preparatory diet the potassium intake was decreased to 50 meq.

Period II was of five days' duration, and the intake during this period was similar to that during Period I except that the intravenous fat supplement was discontinued and the carbohydrate content (and, accordingly, the caloric content) of the oral diet was increased to compensate for the small quantity of carbohydrate present in the fat emulsion preparation.

Results in Experiment 2 (Table I and Fig. 2): During the first period, nitrogen balances were always negative, and the nitrogen deficit averaged −3.38 ± 1.12 Gm. per day. The potassium balance was slightly negative during Period I and averaged −4.25 ± 3.59 meq. per day. Body weight steadily declined, and the weight loss for Period I was 1.5 kilograms. Sodium balances were inconstant, and the net sodium balance for Period I was +50 meq. The K:N ratio of the balance was approximately 1:1.

Period II did not disclose any appreciable change in nitrogen balance. The nitrogen deficit for the five-day period averaged −3.36 ± 0.64 Gm. per day. The potassium deficit increased in Period II and averaged −21 ± 3.80 meq. per

TABLE I. STATISTICAL COMPARISON OF MEAN NITROGEN AND POTASSIUM BALANCES IN TWO NORMAL SUBJECTS GIVEN FAT EMULSIONS INTRAVENOUSLY

EXPERIMENT	PERIOD	DAYS OF PERIOD	ORAL CALORIES (AV./DAY)	CALORIES FROM IV FAT (AV./DAY)	MEAN NITROGEN INTAKE (GM./DAY)	MEAN NITROGEN BALANCE (GM./DAY)	DIFFERENCE BETWEEN COMPARED MEANS	MEAN POTASSIUM INTAKE (MEQ./DAY)	MEAN POTASSIUM BALANCE (MEQ./DAY)	DIFFERENCE BETWEEN COMPARED MEANS
1. Constant marginal protein intake	I and III	12	947	0	7.8	−2.90 ± 1.20	1.74*	59.3	−17.55 ± 6.98	15.47†
	II	5	884	930	7.8	−1.16 ± 1.09		56.0	− 2.08 ± 11.66	
2. Constant inadequate protein intake	I	4	1,423	1,200	3.0	−3.38 ± 1.07	0.02‡	45.0	− 4.25 ± 3.59	16.75†
	II	5	1,520	0	3.0	−3.36 ± 0.64		48.0	−21.0 ± 3.80	

*Difference statistically significant by Student's "t" test at the 0.05 level ($P<0.02$).
†Difference statistically significant by Student's "t" test at the 0.01 level ($P<0.01$).
‡Difference not statistically significant.

day. The K:N deficit ratio for Period II was 6:1. The net sodium balance in Period II was −11 meq., and the weight loss was 1.2 kilograms.

A statistical comparison of the mean nitrogen and potassium balances for Periods I and II is given in Table I.

II. *Surgical Patients.*—

Experiments 3 and 4. Effect of intravenous fat on the "catabolic" response to surgery: Subjects G. P. (aged 43 years, weight 67.4 kilograms) and F. M. (aged 41 years, weight 60.2 kilograms) are considered together since they presented similar clinical problems and were studied in the same way. Both were male patients, and each gave a history of having had duodenal ulcer with symptoms of long standing. However, despite the chronic nature of their illnesses, neither patient appeared poorly nourished.

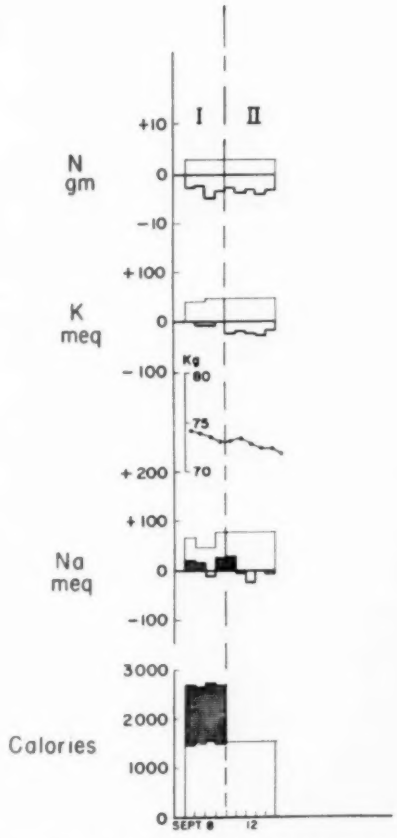


Fig. 2.—Influence of intravenously given fat emulsion on potassium and nitrogen balances in a normal subject on a constant, nitrogen-low intake. Experiment 2.

Both patients were studied after admission to the hospital for subtotal gastrectomy. Each subject was given a small "test" dose of intravenous fat soon after entry into the hospital. Then, in the twenty-four-hour period following surgery and for five to seven days after operation, both subjects were given daily infusions of fat emulsion. The quantity of fat so administered provided up to 2,200 extra calories per day to the patients. F. M. received an

TABLE II. METABOLIC FINDINGS IN A SURGICAL PATIENT GIVEN FAT EMULSIONS INTRAVENOUSLY DURING THE EARLY POSTOPERATIVE PERIOD

(PATIENT G. P., AGED 43 YEARS, MALE. OPERATION: SUBTOTAL GASTRECTOMY)

DATE	BODY WEIGHT (KG.)	CALORIES		NITROGEN (GM.)				POTASSIUM (MEQ.)					SODIUM (MEQ.)					EOS./ MM.^{3}	BODY TEMPERATURE (° F.)
		TOTAL CALORIES	FROM IV FAT	ORAL INTAKE	URINE	STOOL	BALANCE	P.O.	IV	URINE	STOOL	BALANCE	P.O.	IV	URINE	STOOL	BALANCE		
5/19	67.4	3,892	663	21.6	15.46	2.41	+ 3.73	91.5	—	57	20.0	+14.5	150	—	48	2.5	+ 99.5	38	97 -98
5/20	67.2	3,345	—	24.7	20.78	—	– 3.76	107.0	—	64	3.6*	+39.4	158.3	—	142	25.4*	– 9.1	—	97^2-100^4
5/21	Operation	1,583	1,325	—	6.99	—	– 8.20	—	1.2	71	4.0*	–73.8	—	41.2	39	72.4*	– 60.2	—	98 -100^5
5/22	—	1,825	1,325	—	13.70	—	–14.77	—	40	79	7.4*	–46.4	—	77.6	44	88.4*	– 54.8	—	98^6-100^5
5/23	67.0	1,825	1,325	—	9.49	—	– 9.58	—	40	31	0.4*	+ 8.6	—	155.2	33	4.9	+117.3	78	98^6-99^8
5/24	66.2	1,625	1,325	—	9.08	—	– 9.08	—	40	32	—	+ 8.0	8.0	—	41	—	– 33.0	—	99 -99^6
5/25	65.4	1,740	1,325	1.6	13.15	—	–11.55	10.1	40	40	—	+10.1	6.3	—	41	—	– 34.7	125	98^2-99^4
5/26	65.2	2,231	994	6.2	7.55	1.14	– 2.49	44.0	—	30	13.8	+ 0.2	44.4	—	18	1.4	+ 25.0	—	98^2-98^8
5/27	65.1	1,824	—	9.4	16.14	—	+ 6.70	46.5	—	37	—	+ 9.5	46	—	20	—	+ 26.0	—	98 -98^8
5/28	64.7	2,034	—	17.6	12.83	1.00	+ 3.80	70.4	—	53	15.8	+ 1.6	90.2	—	33	1.5	+ 55.7	225	97^8-98
5/29	64.6	2,655	—	22.4	17.00	1.54	+ 3.90	79.0	—	63	12.1	+ 3.9	121.3	—	55	4.0	+ 62.3	—	98 -98
5/30	64.7	2,688	—	21.2	13.83	1.22	+ 6.10	71.0	—	53	6.9	+11.1	127.3	—	80	7.8	+ 39.5	—	96^6-98^5
5/31	65.2	2,256	—	20.1	13.10	1.02	+ 6.0	54.6	—	63	7.6	–16.0	67.2	—	76	8.7	– 17.5	125	97^5-98^3
6/1	65.2	2,422	—	16.8	11.80	0.18	+ 4.8	71.5	—	65	0.5	+ 6.0	134.9	—	65	0.3	+ 69.6	100	97^5-97^5
6/2	65.3	2,771	—	19.5	11.76	0.84	+ 6.9	51.3	—	69	6.7	–24.4	123.1	—	58	3.9	+ 61.2	—	97^2-97^5
6/3	65.3	2,858	—	19.5	14.48	0.87	+ 4.1	83.0	—	34	5.2	+43.8	85.9	—	78	8.2	– 0.3	—	97 -98^1
6/4	65.8	2,709	—	17.6	17.10	0.42	+ 0.1	73.6	—	74	3.4	– 3.8	93.3	—	90	3.7	– 0.4	100	98 -98^1

*Gastric aspiration (meq.).

average of 1,392 calories per day over an eight-day period from this source. G. P. was given an average of 1,270 calories per day for six days in the form of intravenous fat emulsion. In addition to the infusions of fat emulsion, infusions of 5 per cent dextrose in water were given for the first five days after operation. G. P. obtained an average of 360 calories per day in the form of dextrose; F. M. got only 130 calories per day from this source. In each case, oral intake of food was negligible for the first three days after operation. After this time, oral food intake increased gradually, and the infusions of fat were continued until the oral intakes caught up to and exceeded the caloric value of what was being given intravenously. Oral intakes approached normal after about one week postoperatively. By means of the intravenously given fat emulsions, it was possible to maintain the early postoperative caloric intakes of both patients in the range of 1,800 to 2,000 calories per day. No attempt was made to administer intravenous nitrogen and, accordingly, the nitrogen intake during this time was minimal.

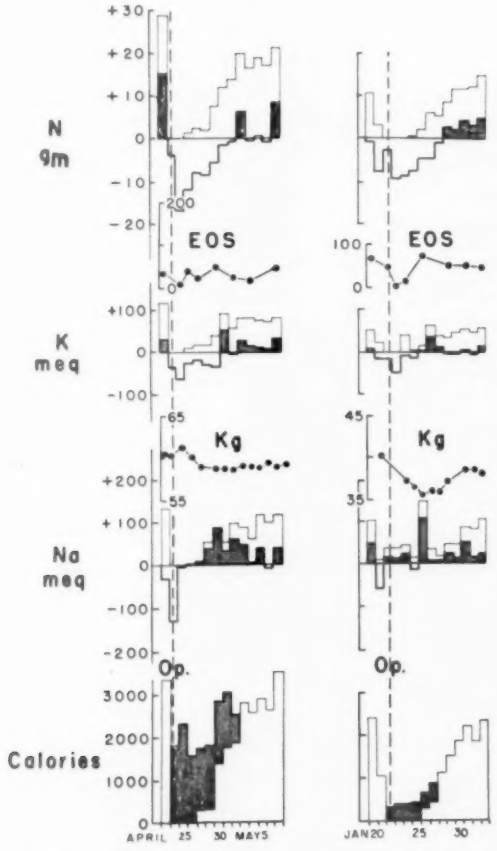


Fig. 3.—Comparison of metabolic responses to subtotal gastrectomy with and without caloric supplementation by means of intravenously administered fat. Experiments 3 and 4.

Results in Experiments 3 and 4 (Table II and Fig. 3): Both patients displayed nitrogen deficits which averaged approximately −9 Gm. per day during the six-day period immediately following surgery. Previous studies on well-

nourished individuals undergoing surgery of similar magnitude indicate that the negative nitrogen balances shown by these two subjects fall within the anticipated range for patients passing through the period of relative caloric starvation which usually follows major gastrointestinal surgery.[11] For purposes of comparison, the balance chart of a well-nourished individual who was subjected to subtotal gastrectomy and who received conventional postoperative nutritional care is shown alongside the balance chart of F. M. in Fig. 3. The metabolic results for G. P. are given in Table II.

The early negative potassium balances which were transient, the sodium "saving," and the weight loss (in the order of 1.5 to 2.0 kilograms) which occurred in both of the patients who were given intravenous fat postoperatively all were characteristic of the metabolic pattern ordinarily observed after subtotal gastrectomy and other surgical procedures of similar magnitude.

DISCUSSION

In Experiment 1 an attempt was made to demonstrate in man the nitrogen- and potassium-sparing properties of a suitably prepared intravenous fat emulsion. As a result of experience gained from earlier studies on the nutritional value of oral fat emulsions, the volunteer subject was maintained on a constant marginal protein intake throughout the entire experiment.[12] At the same time, the constant caloric intake was held well below requirement levels. It was believed that under these conditions, the nitrogen balance might provide a sensitive index to the effect of a calorigenic preparation such as intravenous fat emulsion upon protein metabolism.

Prior to administration of the intravenous fat, the nitrogen deficit (during Period I) averaged -3.36 ± 0.75 Gm. per day. During the five-day period when daily fat infusions were given, the negative nitrogen balance fell to an average of -1.16 ± 1.09 Gm. per day. When the fat was discontinued, the nitrogen deficit again increased to an average of -2.24 ± 1.48 Gm. per day. Even these results may not fully indicate the favorable influence of the intravenously given fat since the nitrogen-sparing effect of the fat appears to have been exerted for one day after the fat was stopped. Changes in potassium balance roughly paralleled the changes in nitrogen balance.

When statistical comparison is made of the mean nitrogen balances of the control and experimental periods (Periods I and III versus Period II), the reduction in the nitrogen deficit during the second period is found to be significant at the 0.05 level. When similar comparison is made with respect to the potassium balances, the decrease in potassium deficit associated with intravenous fat administration is found to be significant at the 0.01 level.*

In Experiment 2 the metabolic effects of intravenously given fat were studied in a second normal subject. However, in this instance the nitrogen

*Previous studies on animals given C^{14}-labeled emulsified triglycerides intravenously suggest that such preparations may continue to be metabolized for a variable period of time after administration of them is complete.[5] Hence, the results on the first day of Period III may have been influenced to some extent by the fat injected on the previous day. It is evident that the nitrogen balance trend in Period III is increasingly negative (Fig. 1). A priori reasoning dictates that Period III, although too brief to be significantly different from Period II with respect to nitrogen balance, should be grouped with Period I for purposes of comparison with Period II. Statistically there is no evidence to the contrary, for when the means of the nitrogen balances for Periods I and III are compared (t test), they do not differ significantly. The same is true of the potassium balances.

intake was kept at a very low level (3 Gm. per day), and for four days prior to the beginning of the experiment the subject was maintained on a nitrogen-low diet designed to adapt him more rapidly to a low nitrogen intake.

By means of fat emulsions administered intravenously, the basic constant oral intake of 1,500 calories per day was augmented by approximately 1,200 calories per day for four days. However, no significant difference in mean nitrogen balance was observed after the caloric intake was decreased markedly as a consequence of discontinuance of the intravenous fat. A striking increase in potassium deficit was observed; the difference in potassium balance between Period II and Period I was significant at the 0.01 level.

Although the intravenous fat supplement did not significantly diminish nitrogen excretion in this brief experiment, it should be pointed out that at low levels of nitrogen intake, decreases in caloric intake ordinarily must be quite large before an appreciable increase in protein catabolism is observed.[13, 14] The potassium saving which seemed to accompany fat administration is difficult to interpret, particularly since the K:N ratio of the diet was abnormally high (16:1). The increase in potassium excretion after discontinuance of the intravenous fat suggests that a shift of potassium out of cells was rapidly taking place without a proportionate increase in cellular breakdown. The high K:N deficit of 6 meq. of potassium to 1 Gm. of nitrogen which occurred in Period II supports this interpretation.

In the early postoperative period, a variety of influences determines the net metabolic response to surgery: principally, these include the "stress" of the procedure and the accompanying immobilization and starvation. The nutritional state of the subject prior to surgery is also an important determining factor. Metabolic responses remarkably similar to those which occur after surgical trauma have been reproduced by means of "mock operation" experiments on normal volunteer subjects.[11] It has been shown that starvation alone produces a metabolic picture distinct from that which follows surgery.[11] The effect of caloric intake upon the biologic response to surgery and injury also has been studied.[15, 16] Indeed, many investigators have wondered whether the loss from the body of nitrogen and potassium which immediately follows injury or surgery might not be related to the short period of starvation that inevitably occurs under such circumstances. Yet, no one appears to have demonstrated unequivocally that the maintenance of a high caloric intake will modify these metabolic changes.

For this reason, a group of patients undergoing subtotal gastrectomy were given enough fat intravenously for the six- to eight-day period following surgery (inclusive of the operative day) to keep their daily caloric intakes in the 1,800 to 2,000 range during this time. Studies on two such subjects (Experiments 3 and 4) are reported here and compared with a third, control study (J. H.) in which a similar operation was performed and a conventional postoperative nutritional regimen was carried out (Fig. 3). The experimental and control regimens differed only with respect to caloric intake. In all three instances, protein intakes were negligible on the operative day and for four days after operation. On the day of operation and for four days thereafter

the control subject received virtually all of his calories in the form of intravenously given dextrose. His average energy intake for this period was approximately 400 calories per day.

It was apparent from these studies on surgical patients that the extra calories from intravenous fat did not appreciably alter the "normal" response pattern to the surgical procedures. Negative nitrogen and potassium balances occurred to a comparable extent in all three cases. Sodium retention in these subjects took place during the first postoperative week irrespective of caloric intake.

It should be pointed out that the two patients given extra calories by means of intravenous fat emulsion still may have been receiving considerably less than their basal requirements following the stress of major surgery even though they were obtaining far more than is usually provided under such circumstances. Whether still higher caloric intakes can alter this "normal" response remains to be determined.

Although a considerable increase in caloric intake immediately after operation and in the early postoperative period does not appear to alter the concurrent metabolic response, it must be emphasized that there exists, nevertheless, a secure place in surgical nutrition for supplementation with intravenous fat and other calorigenic nutrients in the malnourished patient preoperatively and in any patient who, after a week postoperatively, is unable to take adequate amounts of food by mouth. In this later phase of surgical convalescence, an adequate caloric intake is absolutely essential. Without such an intake, positive nitrogen balance is not maintained, and the patient does not regain strength and vigor.[17] It should be remembered that surgical convalescence is a dynamically evolving process: accordingly, evidence that extra caloric provision has failed to alter the nutritional picture in the first days after operation in no way detracts from the crucial importance of providing an adequate caloric intake in the later phases of convalescence.

SUMMARY

Studies on the metabolic effects of 15 per cent fat emulsions administered intravenously to two healthy volunteer subjects and to two surgical patients are described.

In one normal subject on a constant diet inadequate in calories and marginal with respect to protein intake, nitrogen and potassium deficits diminished appreciably when intravenous fat was given, and increased when the period of fat administration terminated.

In a second normal subject on a constant diet inadequate both in calories and protein, no effect of intravenous fat on nitrogen balance was discernible when the caloric intake was decreased by approximately 70 per cent as a result of discontinuance of intravenous fat administration. However, cessation of fat administration was followed by a marked increase in potassium excretion.

Two surgical patients who underwent subtotal gastrectomy were given enough intravenous fat for the six-day period following surgery (inclusive

of the operative day) to maintain their daily caloric intakes in the 1,800 to 2,000 calorie range. The extra calories from this source did not measurably alter the characteristic metabolic response pattern to this type of surgical procedure.

The importance of caloric provision in the later phases of surgical convalescence is discussed.

Acknowledgment.—We record with appreciation the assistance of Mrs. Phyllis B. Michelsen, Division of Biostatistics, School of Public Health, Columbia University, New York, in the preparation of the statistical material presented in this report.

REFERENCES

1. Baba, T.: Ueber den Abbau direkt infundierten Fetts im Tierkörper; II. Mitteilung. Grundumsatz pankreasdiabetischer Tiere nach Fettinfusion, Tohoku J. Exper. Med. **17:** 274, 1931.
2. McKibbin, J. M., Ferry, R. M., Jr., and Stare, F. J.: Parenteral Nutrition. 2. The Utilization of Emulsified Fat Given Intravenously, J. Clin. Investigation **25:** 679, 1946.
3. Mann, G. V., Geyer, R. P., Watkin, D. M., Smythe, R. L., Dju, D., Zamchek, N., and Stare, F. J.: Parenteral Nutrition. 7. Metabolic Studies on Puppies Infused With Fat Emulsions, J. Lab. & Clin. Med. **33:** 1503, 1948.
4. Geyer, R. P., Chipman, J., and Stare, F. J.: Oxidation in Vivo of Emulsified Radioactive Trilaurin Administered Intravenously, J. Biol. Chem. **176:** 1469, 1948.
5. Lerner, S. R., Chaikoff, I. L., and Entenman, C.: Fate of C^{14} Labeled Palmitic Acid Administered Intravenously as a Tripalmitin Emulsion, Proc. Soc. Exper. Biol. & Med. **70:** 384, 1949.
6. Geyer, R. P., Watkin, D. M., Matthews, L. W., and Stare, F. J.: Parenteral Nutrition 11. Studies With Stable and Unstable Fat Emulsions Administered Intravenously, Proc. Soc. Exper. Biol. & Med. **77:** 872, 1951.
7. Gorens, S. W., Geyer, R. P., Matthews, L. W., and Stare, F. J.: Parenteral Nutrition 10. Observations on the Use of a Fat Emulsion for Intravenous Nutrition in Man, J. Lab. & Clin. Med. **34:** 1627, 1949.
8. Neptune, E. M., Geyer, R. P., Saslaw, I. M., and Stare, F. J.: Parenteral Nutrition 12. The Successful Intravenous Administration of Large Quantities of Fat Emulsion to Man, Surg., Gynec. & Obst. **92:** 365, 1951.
9. Dunger, R.: Eine einfache Methode der Zahlung der eosinophilen Leukozyten und der praktische Wert dieser Untersuchung, München. med. Wchnschr. **57:** 1942, 1910.
10. Bowes, A. D., and Church, C. F.: Food Values of Portions Commonly Used, ed. 7, Philadelphia, 1951, College Offset Press.
11. Moore, F. D., and Ball, M.: The Metabolic Response to Surgery, Springfield, 1952, Charles C Thomas, Publisher.
12. Van Itallie, T. B., Logan, W. B., Smythe, R. L., Geyer, R. P., and Stare, F. J.: Fat Emulsions for Oral Nutrition IV. Metabolic Studies on Human Subjects, Metabolism **1:** 80, 1952.
13. Swanson, P. P.: Influence of Nonprotein Calories on Protein Metabolism, Fed. Proc. **10:** 660, 1951.
14. Munro, H. N.: Carbohydrate and Fat as Factors in Protein Utilization and Metabolism, Physiol. Rev. **31:** 449, 1951.
15. Werner, S. C., Habif, D. V., Randall, H. T., and Lockwood, J. S.: Postoperative Nitrogen Loss: a Comparison of the Effects of Trauma and of Caloric Readjustment, Ann. Surg. **130:** 688, 1949.
16. Cuthbertson, D. P.: Further Observations on the Disturbance of Metabolism Caused by Injury, With Particular Reference to the Dietary Requirements of Fracture Cases, Brit. J. Surg. **23:** 505, 1936.
17. Moore, F. D.: Bodily Changes in Surgical Convalescence I. The Normal Sequence. Observations and Interpretations, Ann. Surg. **137:** 289, 1953.

INTUSSUSCEPTION

IRA S. GOLDENBERG, M.D., NEW HAVEN, CONN.

(From the Department of Surgery, Yale University School of Medicine, and the Grace-New Haven Community Hospital)

INTUSSUSCEPTION has been recognized for many years as one of the acute abdominal emergencies which is amenable to cure by prompt surgical intervention. Hunter as early as 1789[3] described in detail a post-mortem specimen of intussusception from a child, but the first report of the successful surgical management in an infant did not appear until 1873.[7] Although intussusception occurs in all age groups, it is principally a disease of childhood and, more particularly, of infancy.

Any discussion of intussusception is most disappointing because there are so many aspects of the disease which are unexplained. A marked predominance of males is reported in almost all series, and a seasonal incidence is apparent in many, the largest number of intussusceptions occurring during the warm months. Particularly puzzling is the lack of definite etiology in almost all cases of childhood intussusception. In adults, however, a lesion involving the bowel wall, such as tumor or a Meckel's diverticulum, can be implicated as the inciting agent. Enlarged lymph nodes in the region of the terminal ileum have been found in many cases in children at operation. It has never been proved, however, whether this lymphadenopathy is cause or result. Perrin and Lindsay[6] first called attention to the possible role played by swollen patches of lymphoid tissue in the wall of the terminal ileum, which are most pronounced in infants less than 1 year of age. Peristaltic waves passing through the segment of bowel so involved attempt to propel the masses in the wall distally as a bolus of fecal material would be moved. Unable to accomplish this because the lymphoid material is within the wall and not within the lumen of the ileum, the peristalsis causes the bowel to fold over on itself, and an intussusception is started.

Any segment of small or large bowel may be involved in an intussusceptive process, but the region of the ileocecal valve is the most common, with progression often to involve ascending and transverse colon. The pathology present is the result of mechanical factors with resulting bowel reaction. When the intussusceptum is firmly held by the intussuscipiens, the lymphatic vessels and veins of the bowel wall are compressed, and edema of the wall results. Acute inflammatory cells respond to the insult and add to the congestion. The process to this point is completely reversible and, if interrupted, the bowel will quickly return to its normal state. If, however, compression of the bowel wall continues, the arterial supply will be embarrassed, and irreversible necrosis will follow. The acute nature of the disease can thus be understood easily, and it

Received for publication Jan. 25, 1954.

is not difficult to see why prompt therapy to reduce the invaginated bowel is imperative. A few hours' delay can easily lead to gangrenous bowel.

Such characteristic pathology must result in a definite clinical picture. The quartet of colicky intermittent abdominal pain, vomiting, blood per rectum,

Fig. 1.—A good illustration of the crescent-shaped defect produced in a case of intussusception as the barium column reaches the most distal portion of the intussuscepted bowel.

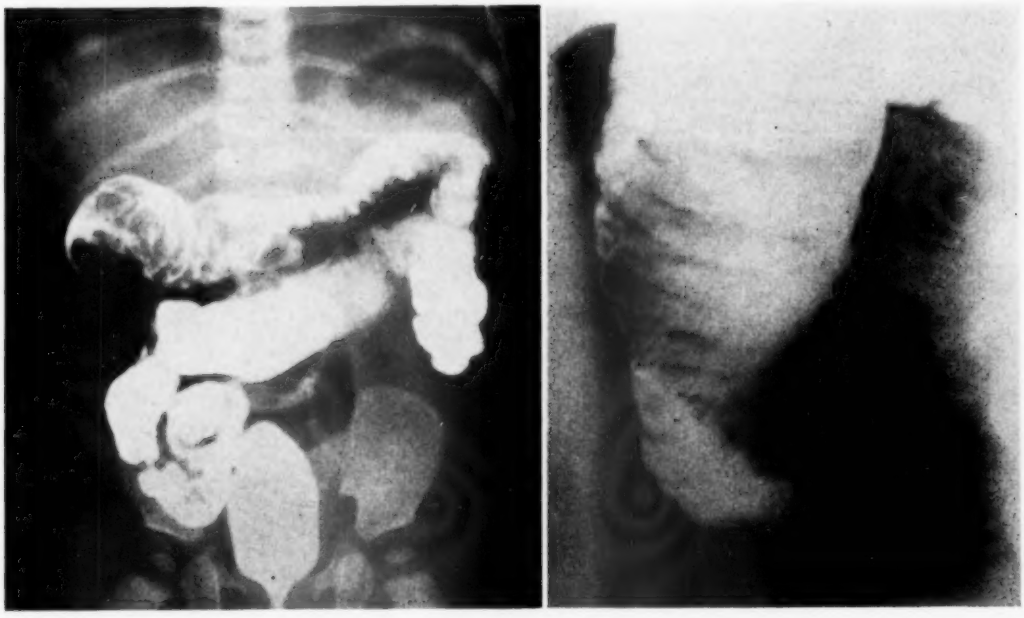
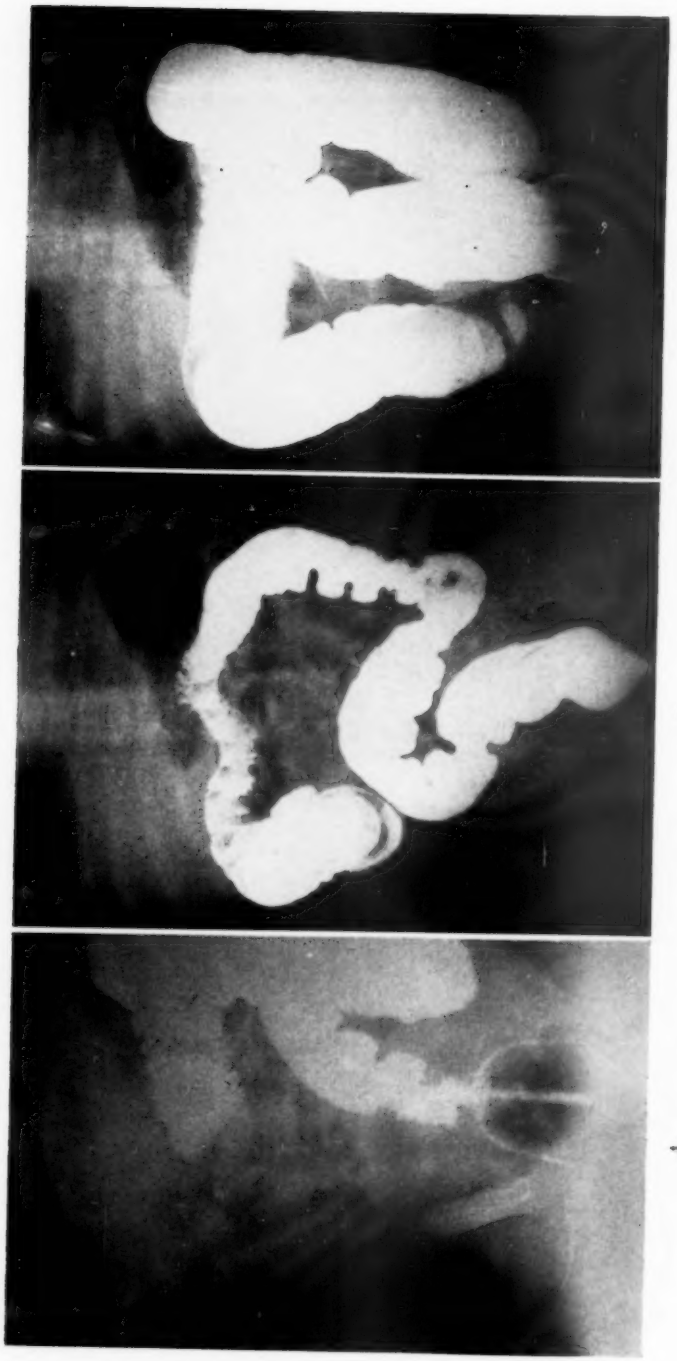


Fig. 2.—Two examples of the coiled spring effect seen in barium enemas in cases of intussusception when the opaque medium dissects between the layers of the invaginated bowel. The film on the right is that of a 16-year-old girl with Hodgkin's disease in the ileum.



A. *B.* *C.*

Fig. 3.—Successive stages in the reduction of an intussusception during a barium enema. The column of barium first encounters resistance in the transverse colon (*A*). The defect is forced proximally (*B*), and barium finally enters the ileum (*C*).

and a palpable abdominal mass has been described. These signs and symptoms can be related with ease to the progressive sequence of intra-abdominal events already described. Dance's signs, which is a sensation of emptiness in the right lower abdominal quadrant due to the absence of the terminal ileum and cecum which have intussuscepted, has been described in many patients, but is usually unreliable.

A plain roentgenogram of the abdomen is somewhat helpful, for small bowel obstruction is often evidenced by dilated loops of small bowel, often with fluid levels as well. A cautious barium enema commonly reveals a crescent-shaped defect at the head of the intussusception (Fig. 1), and a coiled spring effect is sometimes noted as the barium dissects between the layers of the intussusception (Fig. 2). It is not unusual for a diagnostic barium enema to become a form of specific therapy in this disease, a form of therapy which should be tried in all suspected cases before surgery is employed. An intussusceptum which is loosely held will often be reduced as the barium flows into the colon and contacts the head of the bowel column (Fig. 3). It is agreed generally that no more than three feet of hydrostatic pressure should be used in a barium enema when intussusception is suspected lest perforation of the edematous, friable bowel wall occur. Kahle[4] emphasized that any attempted reduction by barium enema should be carried out only with the consent and in the presence of a surgeon. Provisions should be made for immediate surgical intervention if the enema fails or some untoward event such as bowel perforation ensues. Clinical improvement following an enema does not necessarily mean cure, and radiologic evidence of complete reduction is the only sign which can be relied upon, as has been shown in one large series of patients.[5] Successful reduction is determined by entrance of the barium into the small bowel, return of the barium with feces or flatus, and disappearance of the abdominal mass.[8] Ravitch[8] described a quick follow-up test to the barium enema to prove reduction. Powdered charcoal is deposited in the stomach via tube, and six hours later an enema is given. If charcoal is recovered, the completeness of the reduction is assured.

During the period preceding any therapy, first attention, of course, should be given to the general condition of the patient; proper fluid and electrolyte correction of deficiencies due to vomiting should be accomplished. Fluid replacement can be overdone, however, and caution and good judgment should be used in determining the type and amount of fluid to be given. These patients benefit from gastric aspiration, which helps prevent fatal aspiration of stomach contents.[4]

In the event that a barium enema fails to cure the patient, laparotomy should be carried out without hesitation. A McBurney incision commonly is adequate for most cases of intussusception. A right rectus incision offers better exposure, especially if the intussusception has extended into the upper ascending or transverse colon, or a transverse supraumbilical incision can be employed.[4] If the intussusception is of short duration, simple milking of the bowel with careful manipulation may reduce the invagination. Great care should be taken in handling the bowel, for it is friable, and perforation is a real danger. Every

effort must be made to avoid bowel resection because of its added mortality risk, and all the usual restorative measures should be employed before any decision to resect is made. It is logical and most important to make the procedure as brief as possible and to shorten the anesthetic time for these seriously ill patients, yet some surgeons feel that appendectomy should be performed at the time of reduction to cause adhesions in the ileocecal area, preventing further episodes of intussusception. Other procedures directed at bowel fixation have been uniformly unsuccessful and attended with a high mortality in the past.[4]

Sometimes no therapy is needed because spontaneous reduction may occur with clinical improvement and clearing of all signs and symptoms of the disease. It should be pointed out, however, that if there is any doubt in regard to the status of the bowel, exploration should be undertaken without delay.

CASE REPORTS

From 1942 through 1953 inclusive, there were thirty-seven cases of bowel intussusception in thirty-four patients on the University Surgical Service of the Grace-New Haven Community Hospital. Male patients comprised 60 per cent of the total group. All but four patients were children under 5 years of age, and of this group, 73 per cent were less than 24 months old. In relating details of the present group, thirty-seven cases will be considered.

Previous reports of this disease have emphasized the importance of rapid diagnosis and therapy. Delay between onset of symptomatology and treatment has been held responsible for the high mortality so commonly encountered. In the present series, twenty-two patients had symptoms of less than twenty-four hours before being seen by the hospital staff for the first time, and 60 per cent of these had symptoms less than twelve hours. The four cardinal signs and symptoms of intussusception mentioned earlier had a variable occurrence here. Vomiting was present in 83 per cent of cases, as was also abdominal pain, described as intermittent and colicky in slightly over one-half the patients. Abdominal pain was considered to be present here in those infants who drew their legs up over the abdomen coincidental with crying. An abdominal mass was palpated in 70 per cent, while rectal bleeding was noted in only 53 per cent. Bowel irregularities such as constipation and diarrhea occurred in only four instances during the period immediately preceding and during the intussusceptive episode.

Elevation of temperature greater than 1° F. was present in twenty-one cases, and a leukocytosis with a shift to the left occurred in twenty-seven patients. The elevated temperature and white blood cell count were prominent in those patients who had their symptoms the longest period of time. These findings also correlated well with the degree of intussusception later found at operation. In two patients, symptoms were so atypical of intussusception and so typical of acute gastroenteritis that they were discharged after being seen in the emergency division. Both, however, returned hours later when symptoms became more marked. Each was subsequently explored and, after reduction

of an ileo-ileo-cecal intussusception in one, and an ileo-cecal-colic intussusception in the other, both had uneventful recoveries (Table I).

TABLE I. SIGNS AND SYMPTOMS IN THIRTY-SEVEN CASES OF BOWEL INTUSSUSCEPTION

Abdominal pain	31
Vomiting	30
Abdominal mass	26
Rectal bleeding	19
Fever (over 1° F.)	21
Leukocytosis	27

Survey roentgenograms of the abdomen were interpreted as showing small bowel obstruction in sixteen patients and were suggestive of intussusception in thirteen of these. A barium enema followed the survey films of the abdomen in all cases, and an intussusceptive defect was demonstrated in all of them. Spontaneous reduction of a probable intussusception occurred in two patients, and a barium enema, performed after reduction had evidently taken place, in each was interpreted as negative. Complete reduction of the intussusception was accomplished by only 40 per cent of the barium enemas given. Partial reduction occurred in 21 per cent, and all these patients underwent laparotomy, with reduction accomplished at operation.

Surgical intervention with reduction at operation was employed in a total of twenty-six instances, with resection of gangrenous bowel in three additional patients. Appendectomies were performed in nine of these patients, but no specific procedures to fix the ileocecum to surrounding tissues were carried out in any case.

As discussed earlier, enlarged lymph nodes are commonly found in the mesentery of the terminal ileum in cases of intussusception. In fourteen of the cases, large nodes were described as being present in this area by the surgeon. Such a high incidence points to the possible role played by these nodes in the etiology of the disease. No other possible etiologic factors could be found in any of the childhood cases.

The portion of bowel involved in each case here was clear except in the two children who were not explored because of probable spontaneous reduction. Of the remainder, 6 per cent had ileo-ileal intussusception, 25 per cent were ileo-cecal, 60 per cent were ileo-cecal-colic, and 9 per cent were ileo-ileo-cecal-colic (Table II).

TABLE II. TYPE AND LOCATION IN THIRTY-SEVEN CASES OF BOWEL INTUSSUSCEPTION

Ileo-cecal-colic	20
Ileo-cecal	9
Ileo-ileo-cecal-colic	4
Jejuno-jejunal	1
Ileo-ileal	1
Undetermined	2
Recurrent	3
Postoperative	2
Post-mortem	1

Only one death occurred in the present group. A 2-year-old boy who had symptoms for forty-eight hours was brought to the emergency division, where

the diagnosis was made, but the child died suddenly during induction of anesthesia prior to exploration. Post-mortem examination revealed an ileo-cecal-colic intussusception, with strangulation and gangrene of the intussuscepted portion of ileum.

One of the children in the present series had undergone an operative procedure for hypertrophic pyloric stenosis, and nineteen days postoperatively developed signs of small bowel obstruction. Exploration revealed an ileo-cecal-colic intussusception, which was reduced with ease, and an uneventful recovery ensued. Proved recurrent episodes occurred in three children. The first was an 8-month-old girl who had an ileo-cecal intussusception reduced easily at operation. Seven days later an ileo-ileal intussusception had to be reduced operatively. A second child, aged 2½ years, had two episodes of intussusception within twelve months. The first episode was an ileo-cecal-colic intussusception, which was corrected at operation. Approximately one year later the child was readmitted with a clinical history compatible with intussusception, and a barium enema demonstrated the typical defect at the ileocecal region. The patient was explored again, but the intussusception was already reduced; there was found to be present, however, much evidence of inflammation in the ileocecal region. Another child had an ileo-cecal-colic intussusception reduced easily by barium enema, only to have recurrence two weeks later. In this second instance exploration was necessary, and an ileo-cecal intussusception was reduced.

Of the four adults in this series, one intussusception occurred in the postoperative period in a 53-year-old woman following lysis of pelvic adhesions which had caused small bowel obstruction. The patient was re-explored when symptoms of obstruction developed four days after the lysis, and a jejuno-jejunal intussusception was reduced. No cause for the situation was apparent. The second adult was a 70-year-old woman who had a carcinoma of the cecum as the intussusceptum. A right colectomy was performed, and the patient recovered without event. The third adult was a 53-year-old man with an ileo-cecal intussusception without evidence of other bowel abnormality. This was easily reduced at operation. The last adult in this series was a 16-year-old girl who had right lower quadrant pain for four months and who was shown to have an ileo-cecal-colic intussusception during a diagnostic barium enema. At laparotomy the intussusception could not be completely reduced, and a portion of ileum had to be resected. In the resected specimen there was a 3 cm. in diameter mucosal mass extending through the serosa, which microscopically was shown to be Hodgkin's disease (Table III).

TABLE III. TREATMENT OF THIRTY-SEVEN CASES OF BOWEL INTUSSUSCEPTION

Reduction at operation	26
Resection of bowel	3
Reduction by barium enema	6
Spontaneous reduction (?)	2

The low mortality of one patient in thirty-seven in the present series is somewhat less than has been reported in other recent series.[1, 2, 9, 10] The present

group of cases is small, but is large enough to be used as a measure of therapeutic approaches to the problem. The barium enema as a reducing agent of intussusception is good, but surgical intervention is probably better; it gets to the source of the trouble rapidly and is more certain to lead to complete reduction.

CONCLUSIONS

1. Intussusception is an acute abdominal emergency in which the diagnosis can usually be made easily.

2. Prompt surgical intervention is probably the best therapy; it is swift and certain.

3. Rapid diagnosis and treatment are responsible for the low mortality of 2.7 per cent reported here.

REFERENCES

1. Ferrer, J. M., Jr.: Intussusception in Children and Adults, S. Clin. North America **30:** 515-528, 1950.
2. Gross, R. E., and Ware, P. F.: Intussusception in Childhood, New England J. Med. **239:** 645-652, 1948.
3. Hunter, J.: On Introsusception, London, 1793, Trans. of a Society for the Improvement of Medical and Chirurgical Knowledge, pp. 103-115; (cited in Ravitch.[7])
4. Kahle, H. R., and Thompson, C. T.: Diagnostic and Therapeutic Considerations of Intussusception, Surg., Gynec. & Obst. **97:** 693-701, 1953.
5. Nordentoft, J. M.: The Reduction of Intussusception in Children by Barium Enemata, Acta radiol. **37:** 341-347, 1952.
6. Perrin, W. S., and Lindsay, E. C.: Intussusception; a Monograph Based on 400 Cases, Brit. J. Surg. **9:** 46-71, 1921.
7. Ravitch, M. M.: Jonathan Hutchinson and Intussusception, Bull. Hist. Med. **25:** 342-353, 1951.
8. Ravitch, M. M., and McCune, R. M., Jr.: Intussusception in Infants and Children, J. Pediat. **37:** 153-173, 1950.
9. Snyder, W. H., Jr., Kraus, A. R., and Chaffin, L.: Intussusception in Infants and Children, Ann. Surg. **130:** 200-210, 1949.
10. Ware, G. W., and Coffey, R. J.: Intussusception in Infancy and Childhood, Surg., Gynec. & Obst. **91:** 173-178, 1950.

POTASSIUM MIGRATION IN EXPERIMENTAL BURNS

CLARKE L. HENRY, CAPTAIN, MC, AUS, AND WILLIAM H. AMSPACHER, COLONEL, MC, USA, FORT SAM HOUSTON, TEXAS

WITH THE TECHNICAL ASSISTANCE OF RAYMOND J. LICHTER, B.S.

(From the Surgical Research Unit, Brooke Army Medical Center)

CERTAIN electrolyte shifts in body tissue have been postulated to occur in traumatic shock. Darrow,[1] Rosenthal and Tabor,[2] Walker,[3] and others have contributed basic information on this problem. In burn shock and tourniquet shock in mice, Fox[4] demonstrated changes in potassium, sodium, and water concentrations by a method of total limb analysis.

Tissue analyses without determination of the intracellular and extracellular fluid compartments present serious obstacles to interpretation. The total limb analysis method fails to furnish information on the dynamic nature of the electrolyte exchange. It seemed desirable, therefore, to demonstrate electrolyte interchanges by a method that would not involve the technical and interpretative difficulties of tissue analyses.

This presentation is a report of changing blood stream concentrations of electrolytes in acute burns. A definite response pattern has been established in regard to the time relationship, the increment, and direction of the shifts involved.

EXPERIMENTAL PLAN AND METHODS

Ten healthy mongrel dogs weighing in excess of 15 kilograms were used as experimental animals. The animals were anesthetized by use of intravenous pentobarbital, 0.5 c.c. per kilogram of body weight. Because of the length of the experiment, supplemental smaller doses were required occasionally. The right femoral vessels were exposed, and zero time control blood samples were obtained from both the artery and the vein. These and all subsequent blood samples were collected in heparinized syringes.

A standardized burn was then administered by immersing the left hind limb in water at 100° C. for thirty seconds. Previous trials with postburn observations indicated that a third degree burn would be uniformly obtained by this method. Immediately after burning, the left femoral vessels were exposed, and postburn samples from both the femoral artery and vein were obtained at the following time intervals: ten and thirty minutes, and one, two, three, five, and seven hours. The animals were then placed in cages and allowed to recover. No treatment was given at any time. At twenty-four hours postburn, a single venous sample was obtained from the normal hind limb. Sampling from the four vessels was intentionally random and as nearly

Received for publication, March 3, 1954.

simultaneous as was technically feasible. The total amount of blood withdrawn from each animal over the twenty-four-hour period of observation was approximately 220 c.c.

The hematocrit was determined in all but the ten- and thirty-minute blood samples. The blood was then promptly centrifuged, and the sodium and potassium concentrations of the plasma were measured by use of a Perkin-Elmer Model 52-C Flame Photometer. A moderate, grossly uniform hemolysis was observed in all postburn specimens.

The larger animals presented a distinct technical advantage in that their blood vessels were of greater caliber, and this rendered the multiple sampling procedure less difficult. In addition, the total blood withdrawn represented a relatively small fraction of the total blood volume. For purposes of these experiments, the laboratory animal chosen was the dog because the intra-erythrocyte potassium concentration so nearly approximates that of plasma that even moderate hemolysis has only a negligible effect on the plasma potassium concentration.

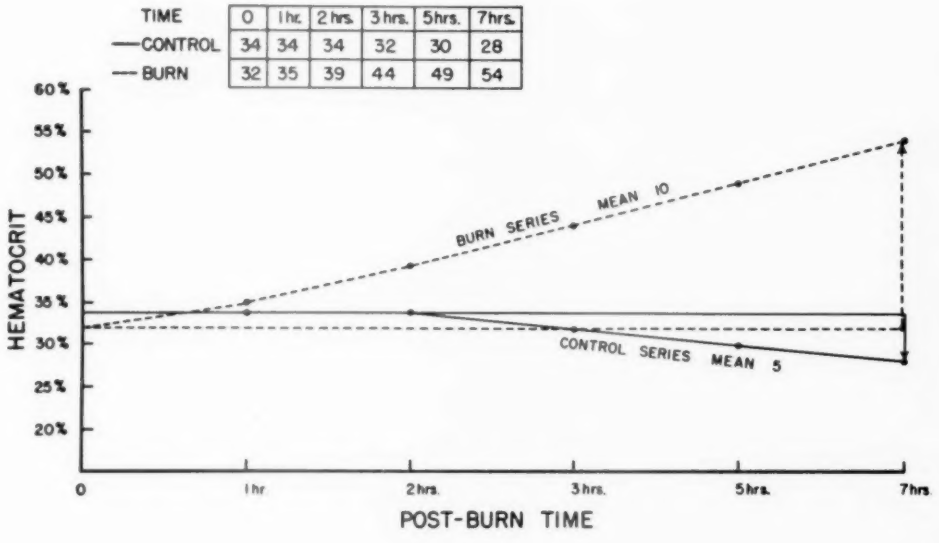


Fig. 1.

In the control series, five healthy mongrel dogs, weighing in excess of 15 kilograms, were subjected to precisely the identical procedure as the ten consecutive burn animals except that no burn was administered.

RESULTS

Hematocrit.—Mean hematocrit determinations were plotted for both the control and burn series and are presented in Fig. 1. The mean hematocrit for the burn series arises in linear fashion from a preburn normal level of 32 per cent to 54 per cent at the end of seven hours. This increase reflects the hemoconcentration secondary to the inflicted burn trauma. In the control series, there is a moderate but steady decline from a preburn level of 34 per cent to

28 per cent at the end of seven hours postburn. This change is consistent with the over-all blood loss incident to sampling and compensatory hemodilution.

Potassium.—In the burn series, there is a progressive rise in plasma potassium concentrations in all postburn samples; definite gradients in concentration are noted between certain vessels sampled at any one time. These changes in concentration generally develop in the thirty-minute to one-hour postburn interval and apparently reach a peak at some point between seven and twenty-four hours. In each instance, the potassium concentration of the twenty-four-hour venous plasma sample approached normal levels. In a subsequent series of similar experiments, twenty-four-hour samples from all four vessels were obtained and found to be equal in regard to plasma potassium concentration, and this concentration was approximately that of preburn levels.

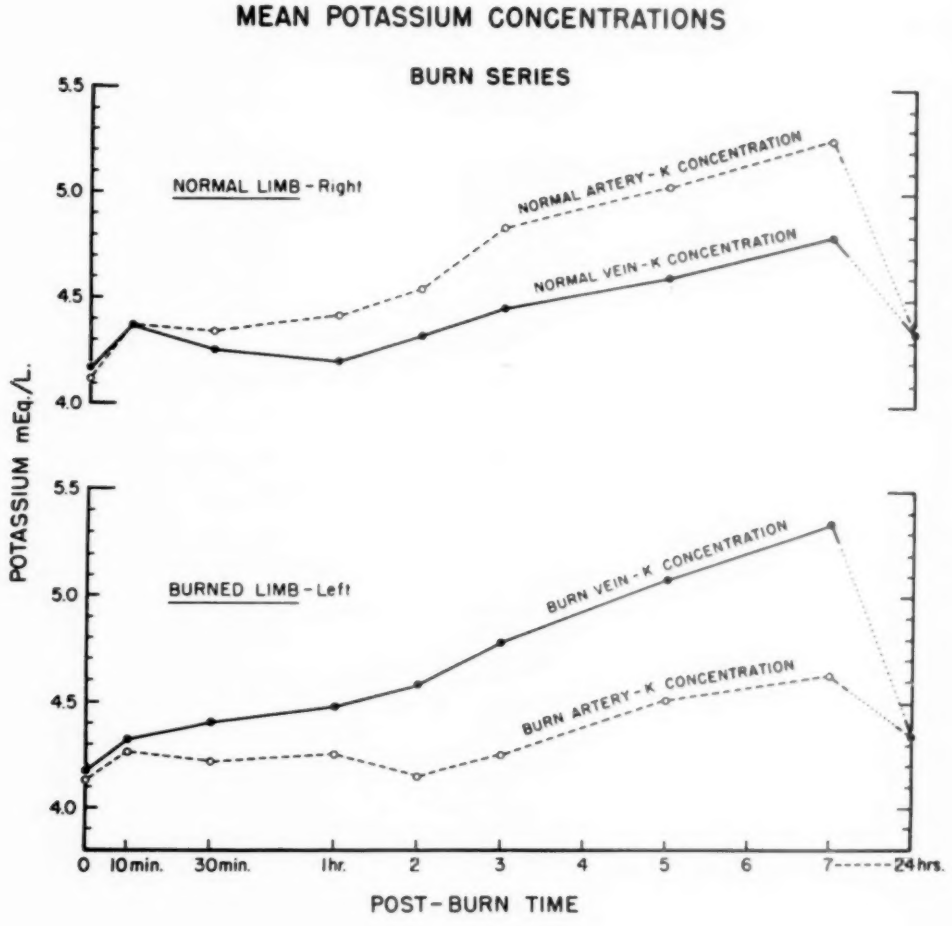


Fig. 2.

Comparison of mean concentration curves of the vessels of the burned extremity reveals a consistently higher potassium concentration in the vein than in the artery (Fig. 2). In the normal limb, this pattern is reversed, and arterial potassium concentrations consistently exceed the venous concentrations.

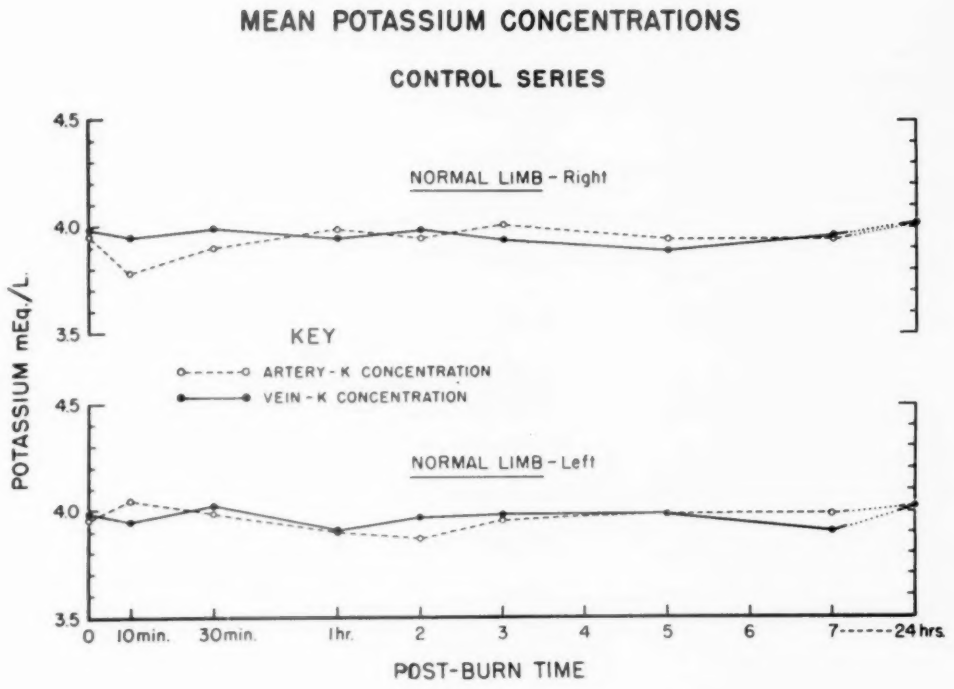

MEAN POTASSIUM CONCENTRATIONS
CONTROL SERIES
NORMAL LIMB - Right
KEY
ARTERY - K CONCENTRATION
VEIN - K CONCENTRATION
NORMAL LIMB - Left
POTASSIUM mEq./L.
4.5
4.0
3.5
0
10min.
30min.
1hr.
2
3
4
5
6
7------24hrs.
POST-BURN TIME

Fig. 3.

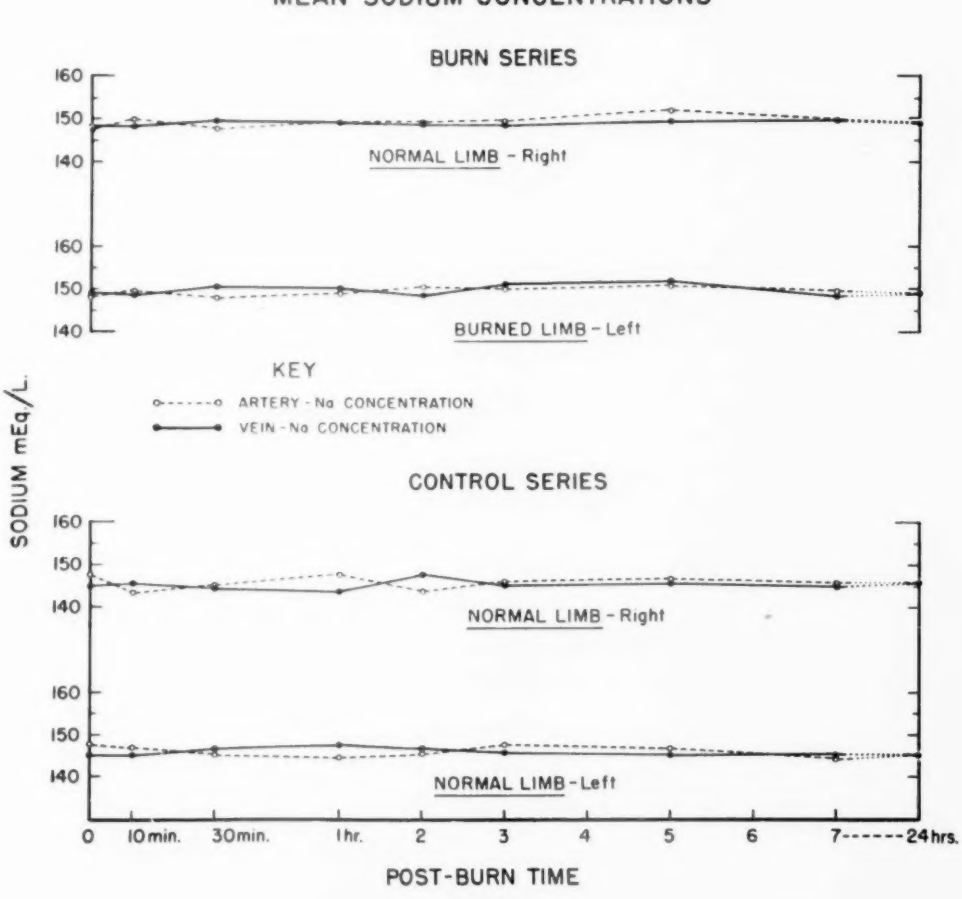

MEAN SODIUM CONCENTRATIONS
BURN SERIES
NORMAL LIMB - Right
BURNED LIMB - Left
KEY
ARTERY - Na CONCENTRATION
VEIN - Na CONCENTRATION
CONTROL SERIES
NORMAL LIMB - Right
NORMAL LIMB - Left
SODIUM mEq./L.
160
150
140
0
10min.
30min.
1hr.
2
3
4
5
6
7------24hrs.
POST-BURN TIME

Fig. 4.

FIG. 5. RAW DATA: CONTROL SERIES

DOG	TIME / VESSEL	0		10 MIN.		30 MIN.		1 HR.		2 HR.		3 HR.		5 HR.		7 HR.		24 HR.	
		A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V
1	Normal	4.00	3.85	3.85	4.00	3.85	4.00	4.00	3.75	4.00	4.00	4.00	4.00	3.85	3.85	4.00	4.00	—	4.00
	Burn	—	—	4.00	4.00	3.85	4.00	3.85	3.85	4.00	3.85	4.00	4.00	4.10	3.85	4.00	4.00	—	—
2	Normal	3.90	4.00	3.75	3.75	3.90	3.75	3.75	3.90	3.75	3.75	3.90	3.75	3.75	3.75	3.75	3.75	—	4.00
	Burn	—	—	3.90	3.75	3.90	3.90	3.75	3.90	3.90	3.75	3.75	3.90	3.75	3.75	3.90	3.75	—	—
3	Normal	3.70	3.90	3.70	3.90	3.70	3.90	3.75	3.75	3.90	3.90	3.90	3.90	3.90	3.75	3.90	3.90	—	4.00
	Burn	—	—	3.90	3.90	3.90	3.90	3.75	3.75	3.90	3.90	3.90	3.90	3.75	3.90	3.90	3.75	—	—
4	Normal	3.90	3.96	3.80	3.90	3.80	3.85	3.94	—	3.90	3.85	3.85	3.85	3.80	3.80	3.90	3.82	—	3.92
	Burn	—	—	3.94	3.90	3.90	3.94	3.85	3.85	3.80	3.90	3.94	3.90	3.90	3.96	3.90	3.85	—	—
5	Normal	4.30	4.20	—	4.20	4.20	4.45	4.35	4.40	4.20	4.45	4.40	4.20	4.40	4.30	4.20	4.35	—	4.20
	Burn	—	—	4.45	4.20	4.20	4.40	4.30	4.20	4.20	4.45	4.35	4.20	4.40	4.45	4.20	4.20	—	—

Mean

Mean—5	TIME / VESSEL	0		10 MIN.		30 MIN.		1 HR.		2 HR.		3 HR.		5 HR.		7 HR.		24 HR.	
		A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V
	Normal	3.96	3.98	3.78	3.95	3.90	3.99	3.99	3.95	3.95	3.99	4.01	3.94	3.94	3.89	3.95	3.96	—	4.02
	Burn	—	—	4.04	3.95	3.98	4.02	3.90	3.91	3.87	3.97	3.96	3.98	3.98	3.98	3.98	3.90	—	—

In the control series, plasma potassium concentrations remain essentially equal in all vessels, and over-all changes in concentration are not observed (Fig. 3).

Sodium.—There is no appreciable alteration in plasma sodium concentrations in the burn or in the control series. The mean curves of sodium concentration for the various vascular channels are flat and practically superimposed (Fig. 4).

STATISTICAL ANALYSIS

Statistical evaluation of the data is accomplished by the use of analysis of variance.[5] This technique is essentially an extension of the familiar t test for the significance of difference between two means that makes possible the joint comparison of many means. The analysis of variance permits separation of the total variation of the data into its component parts, variation due to differences between individual animals, blood vessels sampled, and sampling times. In addition, it allows isolation of the error component, which is essential for the assessment of significance.

FIG. 6. CONTROL SERIES: ANALYSIS OF VARIANCE SUMMARY

SOURCE VARIATION	DEGREES FREEDOM	VARIATION	VARIANCE	F-RATIO	P-VALUE
Column variation (vessels)	3	0.013	0.004	1.651	$P>0.05$
Raw variation (animals)	4	4.696	1.174	437.213	$P<<<0.001$
Replicate error	128	0.962	0.008	2.800	$0.05>P>0.01$
Interaction	12	0.032	0.003	—	—
Total	147	5.704	—	—	—

Control Series.—The raw data for this analysis are reproduced in Fig. 5. Fig. 6 presents a summary of the analysis of variance. For the variation among animals, significance is established at the 0.001 level ($P<<<0.001$). Among the replicate samples drawn from the same animal at different time intervals, there is only borderline significant difference ($0.05>P>0.01$), assuming a level of significance of 0.01. There is also no significant difference among the various blood vessels sampled ($P>0.05$) in any one animal. In Fig. 6, the quantity labeled "interaction" is the basic error or precision term of the total analysis. The square root of this term is the over-all standard deviation and equals 0.0518 meq. per liter. Expressed as a percentage of the over-all mean, this equals 1.31 per cent. This figure of 1.31 per cent represents a most satisfactory precision. The sampling error involved in taking replicates from the same animal is considered by taking the square root of the replicate variance. This figure, 0.0867 meq. per liter, expressed as a per cent of the mean, was found to be 2.19 per cent.

In summary, there are no significant differences in individual animals between various vessels sampled, either with respect to artery or vein, to limb involved, or to time interval at which blood was withdrawn. There is a significant difference among blood levels from different animals.

FIG. 7. RAW DATA: BURN SERIES

DOG	TIME	0		10 MIN.		30 MIN.		1 HR.		2 HR.		3 HR.		5 HR.		7 HR.		24 HR.	
	VESSEL	A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V
1	Normal	3.95	4.10	4.30	4.30	4.20	4.20	4.20	4.35	4.30	4.40	4.70	4.60	4.60	4.65	5.00	4.80	—	4.40
	Burn	—	—	4.40	4.50	4.20	4.20	4.20	4.40	4.30	4.50	4.35	4.65	4.40	4.70	4.50	4.95	—	—
2	Normal	4.85	4.85	4.85	4.93	5.00	4.90	4.65	4.75	4.50	4.20	5.00	4.70	5.00	4.75	5.20	4.85	—	5.35
	Burn	—	—	5.20	5.20	4.80	5.00	4.80	4.80	4.50	4.50	4.15	4.15	5.03	5.20	5.00	5.45	—	—
3	Normal	4.03	4.10	4.40	4.35	4.25	4.45	4.10	4.10	4.45	4.35	4.85	4.55	—	—	—	—	—	4.25
	Burn	—	—	4.10	4.65	4.10	4.55	4.35	4.85	4.25	4.95	4.35	4.95	—	—	—	—	—	—
4	Normal	3.80	4.10	4.30	4.50	4.40	4.10	4.70	4.40	4.80	4.50	5.00	4.30	5.00	4.40	5.20	4.50	—	4.15
	Burn	—	—	4.20	4.00	4.50	4.40	4.40	4.40	4.00	4.50	4.20	4.70	4.40	4.70	4.50	5.00	—	—
5	Normal	3.95	4.00	4.25	4.25	4.35	3.95	4.55	4.30	4.75	4.45	4.80	4.50	4.95	4.60	5.08	4.80	—	4.10
	Burn	—	—	4.25	4.05	3.95	4.25	4.35	4.25	4.45	4.80	4.48	5.15	4.70	5.35	4.85	5.50	—	—
6	Normal	4.06	4.00	4.15	4.10	3.85	4.03	4.30	4.28	4.20	4.10	4.50	4.00	4.80	4.20	4.85	4.40	—	4.05
	Burn	—	—	3.75	3.75	3.80	3.80	4.00	3.90	3.95	4.03	4.10	4.20	4.25	4.45	4.20	4.58	—	—
7	Normal	4.13	4.10	4.40	4.35	4.30	4.45	4.15	4.10	4.50	4.35	4.90	4.55	5.23	4.80	5.30	4.90	—	—
	Burn	—	—	4.08	4.45	4.10	4.55	4.10	4.80	4.35	4.85	4.38	4.95	4.45	5.08	4.65	5.25	—	—
8	Normal	4.35	4.45	4.65	4.30	4.60	4.30	4.90	4.05	4.95	4.40	5.05	4.65	5.55	5.05	6.10	5.35	—	—
	Burn	—	—	4.55	4.75	4.40	4.80	4.05	4.95	4.00	5.10	4.25	5.60	4.60	6.10	—	6.60	—	—
9	Normal	4.00	3.90	4.12	4.30	4.20	4.00	4.44	3.70	4.60	4.10	4.92	4.20	4.98	4.28	—	—	—	4.20
	Burn	—	—	4.05	3.90	4.10	4.30	4.05	4.20	3.80	4.40	4.05	4.90	4.30	5.32	—	—	—	—
10	Normal	4.10	4.00	4.24	4.30	4.20	4.20	4.10	4.00	4.44	4.35	4.70	4.50	5.16	4.70	5.30	4.78	—	4.21
	Burn	—	—	4.20	3.90	4.16	4.20	4.20	4.30	3.90	—	4.20	4.60	4.48	4.94	4.64	5.38	—	—

Mean

Mean—10	TIME	0		10 MIN.		30 MIN.		1 HR.		2 HR.		3 HR.		5 HR.		7 HR.		24 HR.	
	VESSEL	A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V	A	V
	Normal	4.12	4.16	4.37	4.37	4.34	4.26	4.41	4.20	4.54	4.32	4.84	4.46	5.03	4.60	5.25	4.80	—	4.34
	Burn	—	—	4.28	4.32	4.21	4.40	4.25	4.48	4.15	4.58	4.25	4.78	4.51	5.09	4.62	5.34	—	—

Burn Series.—The data from the ten experimental burn animals, as tabulated in Fig. 7, are analyzed. Analysis is first performed with respect to changes in three broad postburn time categories: 0-10 minutes, 30 minutes-1 hour, and 2-7 hours (Fig. 8). These postburn intervals are arbitrarily chosen from the graphic presentation of the data. Significant differences are noted between these three times ($P<<0.001$). Data are also analyzed from the standpoint of the four vessels involved. Summary of this analysis appears in Fig. 9 and indicates over-all significant differences between all four vessels sampled ($P<<0.001$). Because of the importance of this last analysis, two secondary analysis systems were performed to test further the differences between the four vessels.

FIG. 8. BURN SERIES: ANALYSIS OF VARIANCE SUMMARY—TIME INTERVALS

SOURCE VARIATION	DEGREES FREEDOM	VARIATION	VARIANCE	F-RATIO	P-VALUE
Column variation (time intervals)	2	11.150	5.575	29.413	$P<<0.001$
Row variation (animals)	9	12.078	1.342	7.081	$P<<0.001$
Replicate error	261	27.486	0.105	1.800*	$0.05>P>0.01$
Interaction	18	3.412	0.190	—	—
Total	290	54.126	—	—	—

*These figures represent the ratio of interaction to replicate error variance since the replicate error variance is less than interaction variance.

FIG. 9. BURN SERIES: ANALYSIS OF VARIANCE SUMMARY—VESSELS

SOURCE VARIATION	FREEDOM	VARIATION	VARIANCE	F-RATIO	P-VALUE
Column variation (vessels)	3	6.727	2.242	15.356	$P<<0.001$
Row variation (animals)	9	12.079	1.342	9.191	$P<<0.001$
Replicate error	251	31.379	0.125	1.168*	$P>0.05$
Interaction	27	3.942	0.146		
Total	290	54.126	—	—	—

*These figures represent the ratio of interaction to replicate error variance since the replicate error variance is less than interaction variance.

System I (Fig. 10).—Normal artery and normal vein differ with a high level of significance ($P \overset{a}{=} 0.001$). Burn artery and burn vein also show highly significant differences ($P<<0.001$). The sum of normal artery and vein and the sum of burn artery and vein do not show significant differences ($P>0.05$).

FIG. 10. BURN SERIES: ANALYSIS OF VARIANCE SUMMARY—SYSTEM I

	SOURCE VARIATION	DEGREES FREEDOM	VARIATION	VARIANCE	F-RATIO	P-VALUE
Columns	Normal artery vs. normal vein	1	1.697	1.697	11.621	$P \overset{a}{=} 0.001$
Columns	Burn artery vs. burn vein	1	5.016	5.016	34.355	$P<<0.001$
Columns	Burn vein + burn artery vs. normal vein + normal artery	1	0.013	0.013	—	—
	Interaction	27	3.942	0.146	—	—

System II (Fig. 11.)—Normal vein and burn vein were compared and found to differ significantly ($P<<0.001$). Normal artery differs significantly from burn artery ($P<<0.001$). The sum of normal artery and burn artery does not differ significantly from the sum of normal vein and burn vein ($P>0.05$).

FIG. 11. BURN SERIES: ANALYSIS OF VARIANCE SUMMARY—SYSTEM II

	SOURCE VARIATION	DEGREES FREEDOM	VARIATION	VARIANCE	F-RATIO	P-VALUE
Columns	Burn artery vs. normal artery	1	2.925	2.925	20.035	$P<<0.001$
	Burn vein vs. normal vein	1	3.474	3.474	23.791	$P<<0.001$
	Burn artery + normal artery vs. burn vein + normal vein	1	0.327	0.327	2.242	$P > 0.05$
	Interaction	27	3.942	0.146	—	—

One of the conclusions to be drawn from this statistical investigation is that the graphic presentation of data as illustrated in Figs. 2 and 3 is valid. It is clear that the differences seen are of high order of statistical significance. These graphs can, therefore, be accepted as a legitimate summary of the experimental results and represent a sound basis for interpretation.

DISCUSSION

Potassium Data.—Although definite concentration changes of plasma potassium occur as early as ten minutes after the burn, the marked increases appear at approximately one hour. There is no correlation in time or in degree between the appearance of these potassium concentration increases at one hour postburn, and the postburn hemolysis. The hemolysis is uniform throughout, beginning with the ten-minute postburn sample. The gentle upward slope of the rising plasma potassium concentration, the time of appearance in the postburn state, and the lack of correlation with hemolysis suggest that potassium has been released from the injured cells.

The vein of the burned extremity represents the outflow tract from the tissue mass and reflects potassium loss from the site of trauma by increasing concentrations over the parallel inflow arterial concentrations. This pattern of increasing concentration gradient between the two vessels reaches a recorded mean maximum of 0.72 meq. per liter at the seven-hour period. This is indicative of considerable potassium loss from the burned area.

Comparison of the mean potassium concentration curves for artery and vein of the normal limb reveals a complete reversal of pattern; the arterial plasma potassium concentration is consistently elevated above the venous plasma potassium concentration. The resultant gradient of concentrations between the two vessels reaches a recorded mean maximum of 0.45 meq. per liter at the seven-hour postburn period. This gradient indicates that more potassium is entering the limb via the arterial channel than is leaving by way of the venous route and, therefore, that potassium has been deposited in the limb. The 0.45 meq. per liter gradient of deposition into the normal limb is understandably of lesser magnitude than the 0.72 meq. per liter gradient of release

from the burned limb. The normal hind limb represents only one of several sources for deposition of potassium released from the burned member.

Potassium concentrations in plasma from the burn vein remain consistently elevated over those of the opposite vein. This pattern is consistent with the concept of potassium release by traumatized tissues and its pouring into venous return channels. The resultant potassium concentration in burn vein plasma is higher than that venous concentration obtained from the normal limb where its potassium concentration has been subjected to the dilution effect of circulation.

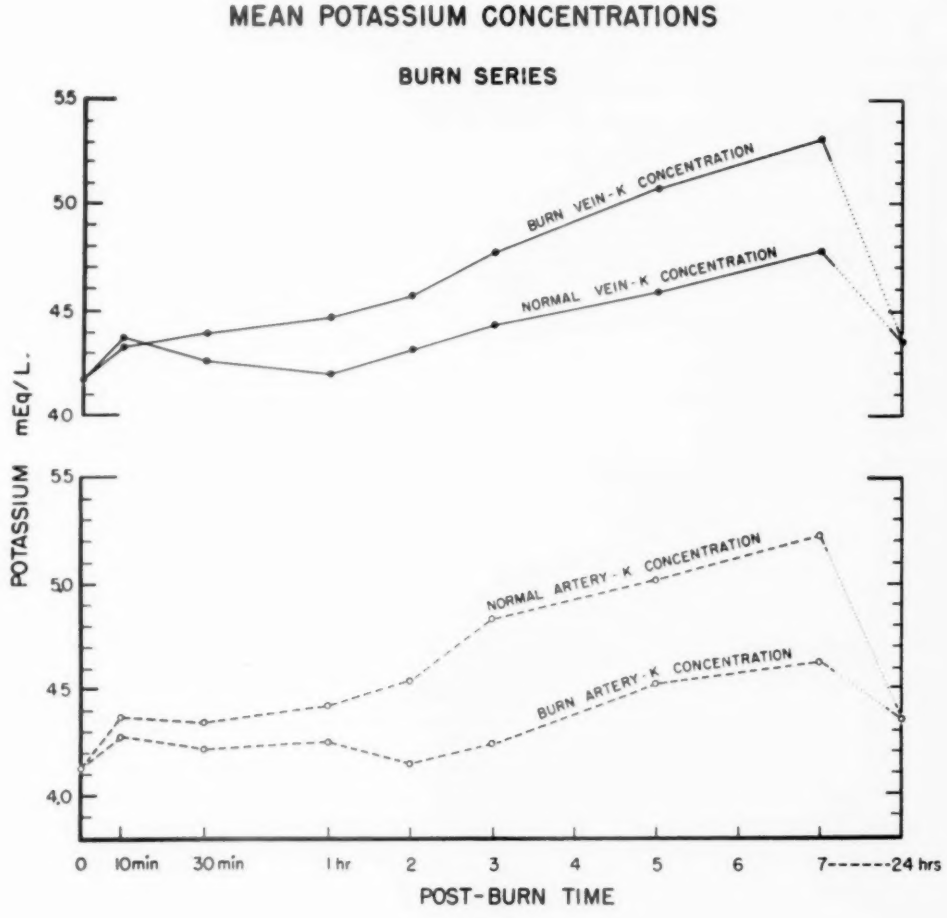


Fig. 12.

One would expect that comparison of the two arterial concentration curves would show them to be quite similar since they originate from a common central source, the abdominal aorta. Such is not the case, however, and the normal artery curve is seen to rise above the burn artery curve. The resultant discrepancy is seen in Fig. 12. This discrepancy, although unexplained at present, represents a statistically significant observation; further investigation is needed on this point.

The logical sequel to this study will be determination of blood flow in these extremities, after which a quantitative approach to the potassium shift will be feasible. Such a study, involving a method of K^{42} equilibration, is at present under way in this laboratory, and will be reported in a subsequent communication.

Sodium Data.—From the data, nothing can be said about sodium shifts except that if the sodium-potassium interchange is on the basis of milliequivalent per milliequivalent, then the transfer of sodium is one too subtle for detection by this approach.

SUMMARY

1. Marked increases in plasma potassium levels occur in experimental acute burns in the dog.

2. On the basis of differential plasma potassium concentration gradients in parallel vascular channels, evidence is presented which substantiates the theory of potassium loss from traumatized tissue and its deposition into normal tissues.

3. A consistent reproducible pattern of plasma potassium concentration changes of statistical significance in burns has been developed. Quantitation of this observed shift pattern awaits development of a satisfactory method of measuring blood flow in the extremity.

4. This response pattern will serve as a base-line control for various therapeutic regimes, the protocols for which are currently being investigated.

Acknowledgments.—We gratefully acknowledge the assistance of Lieutenant Melvin S. Schwartz, who outlined and performed the analysis of variance of all data. For careful criticism of the interpretation of results, and for assistance in editing the manuscript, we are indebted to Captain Eric Reiss.

REFERENCES

1. Darrow, D. C., and Engel, F. F.: Liver Water and Electrolytes in Hemorrhagic Shock, Am. J. Physiol. **145:** 32, 1945.
2. Rosenthal, S. M., and Tabor, H.: Electrolyte Changes and Chemotherapy in Experimental Burn, Traumatic Shock and Hemorrhage, Arch. Surg. **51:** 244, 1945.
3. Walker, J. M.: Potassium, Surgical Aspects: Burns, Advances in Medicine and Surgery, Philadelphia, 1952, W. B. Saunders Company, p. 115.
4. Fox, C. L.: Redistribution of Potassium, Sodium, and Water in Burns, Trauma, and Its Relation to Phenomena of Shock, Am. J. Physiol. **151:** 155-157, 1947.
5. Croxton, F. E.: Elementary Statistics With Applications in Medicine, New York, 1953, Prentice-Hall, Inc.

FACIAL NERVE PARESIS IN PAROTID SURGERY*

S. L. Perzik, M.D., Beverly Hills, Calif.

INTRODUCTION

IN OPERATIONS on the parotid salivary gland, the facial nerve presents a stumbling block to the successful consummation of the surgery. In order to avoid permanent injury to this structure, it is necessary to expose more or less of it in every operation. Invariably such exposure of the facial nerve will result in some degree of paresis. This may be so mild that only on very careful examination with the mouth wide open will the weakness of the more commonly involved lower lip be noted. Usually the paresis is extensive enough to be easily evident, and often it may involve the entire area of facial nerve distribution.

Deductions based on casual observation have frequently been noted regarding the frequency, extent, and recovery from this form of paresis. Often the conclusions thus obtained were directly contradictory. The present study is an attempt to obtain more accurate data based on controlled clinical observation in a large enough series of cases to warrant recognition of the conclusions thus obtained. Fortified beforehand with these clinical data, the operating surgeon can more confidently assure both his patient and himself of the eventual satisfactory outcome of the anticipated and often frightening postoperative paresis.

THE MATERIAL

In 153 cases of parotid surgery, there were 147 in which the surgery included the deliberate exposure and dissection of the facial nerve. In this latter group, some degree of facial nerve paresis resulted in all cases. Ninety-six of these cases were available for study. Twenty-three cases, in which some degree of paresis is still present, were not included in this analysis because it is felt that at least two years must elapse before a persistent paresis can be considered to be permanent. Another group of thirty-four cases, with preoperative paralysis due to previous surgery or disease, was excluded because a proper differentiation of any additional paresis could not be comparatively analyzed. This latter group will be separately studied.

THE PROBLEM

The purpose of the study of these ninety-six cases was to determine what percentage of patients developed temporary paralysis of the facial nerve and to correlate the degree and extent of this paresis with the position of the lesion, the extent of the surgery, the extent of exposure of the facial nerve, the

Received for publication Feb. 15, 1954.

*Presented at the meeting of the Southern California Chapter of the American College of Surgeons, Santa Barbara, California, Feb. 6, 1954.

age of the patient, and the type of lesion, particularly with respect to its infiltrative or well-defined characteristics. The mode of recovery was also studied and correlated with the various factors. Regardless of whether the paralysis appeared to be complete or not, it was considered to be a complication of paresis since there was no evidence at surgery of solution of continuity of the facial nerve in this group of cases. As previously mentioned, those cases in which the nerve was preoperatively paralyzed or transacted during surgery were excluded from this study.

THE CRITERIA

In determining the degree of paresis, a clinical evaluation of one plus (+) to four plus (++++) was assigned to each of the areas studied. Four plus meant complete paralysis of the area under consideration. The extent of the paresis was measured by the number of the following areas involved, namely, the lower lip, upper lip, eyelids, and forehead. In almost all instances, the function of the facial muscles of expression was checked two hours, twenty-four hours, and forty-eight hours postoperatively and thereafter at regular weekly and, later, monthly intervals. Paresis and recovery were both tested by having the patient open the mouth widely, pucker the lips, close the eyelids, and wrinkle the forehead. It was particularly noted that lower lip paresis often escaped detection if the patient was not checked with the mouth wide open. A patient was considered to have completely recovered when the final vestage of paresis disappeared from the last area involved. All the observations were made by one individual in order to avoid a variance in the interpretation of the findings.

LOCATION AND PARESIS

For this study, the lesion was primarily localized in one of four areas in the parotid gland. The majority were in the lower pole of the superficial lobe, and not infrequently the tumor was partially or completely sequestrated out of the lower border of the gland. In a few instances, it was located between the parotid and the submaxillary salivary glands with a definite but often ephemeral attachment to the parotid. A study of Table I reveals that removal of lesions from the lower pole results in extensive paresis in only about 8 per cent of the cases. The pterygoid extension of the superficial lobe contained tumors which were often wedged between the mastoid process and the angle of the mandible, overlying the main stem and first divisions of the facial nerve. In this location, 26 per cent (last two columns, Table I) of the surgery resulted in extensive facial nerve paresis. The lesions in the preauricular area of the superficial lobe yielded extensive paretic involvement in 42 per cent (last two columns, Table I) of the cases. These lesions often were associated with the proximal end of Stensen's duct and were superimposed on the secondary branches of the two major divisions of the facial nerve. The deep lobe tumors were all subjacent to the main stem and the two major divisions of the facial nerve, and surgery here resulted in the greatest extent of paresis, involving the lips and eyelids, or the lips, eyelids, and forehead in 80 per cent of the

cases. On the basis of Table I, one can correlate the extent of the postsurgical paresis with the location of the parotid gland lesion, the most vulnerable site being the deep lobe and next the preauricular area of the superficial lobe, whereas the lower pole offers the most innocuous site.

TABLE I. THE EFFECT OF THE LOCATION OF THE LESION ON THE EXTENT OF THE RESULTING PARESIS

LOCATION OF LESION AND NUMBER OF PATIENTS	EXTENT OF RESULTING PARESIS (PER CENT)			
	LOWER LIP ALONE	LOWER AND UPPER LIPS	LIPS AND EYELIDS	LIPS, EYELIDS, AND FOREHEAD
Lower pole (superficial lobe),* 37	54	27	--	8
Pterygoid portion (superficial lobe), 23	48	26	4	22
Preauricular area (superficial lobe, 19	37	21	5	37
Deep lobe, 17	6	14	30	50

*Remaining lesions yielded no paresis.

SURGERY AND PARESIS

The cases were further studied from the standpoint of the extent of the surgery performed. Those patients treated by enucleation, subtotal parotidectomy, total parotidectomy, and total parotidectomy plus radical neck dissection were considered separately. Since the resulting paresis is mainly associated with surgery in the region of the facial nerve, the total parotidectomies are considered as a single group regardless of whether a radical neck dissection was also performed.

The data in Table II reveal that the surgery was more extensive in the eradication of lesions of the deep lobe (65 per cent) and preauricular area (49 per cent) than in lesions of the pterygoid area (17 per cent) or lower pole of the superficial lobe (11 per cent) of the parotid.

TABLE II. THE EFFECT OF THE LOCATION OF THE LESION ON THE EXTENT OF THE SURGICAL PROCEDURE

LOCATION OF LESION AND NUMBER OF PATIENTS	EXTENT OF SURGERY (PER CENT)				
	ENUCLEATION	SUBTOTAL PAROTIDECTOMY	TOTAL PAROTIDECTOMY		TOTAL PAROTIDECTOMY AND NECK DISSECTION
Lower pole (superficial lobe), 37	2.2	67	8	(11)	3
Pterygoid lobe (superficial lobe), 23	--	83	4	(17)	13
Preauricular area (superficial lobe), 19	--	53	42	(49)	5
Deep lobe, 17	--	35	65	(65)	--

Table III reveals that the more extensive surgery resulted in more extensive facial nerve paresis. Thus the last two columns reveal that total parotidectomy plus radical neck dissection yielded 80 per cent of extensive nerve paresis in its group, the total parotidectomies 65 per cent, and the subtotal parotidectomies 22 per cent.

TABLE III. THE EFFECT OF THE EXTENT OF THE SURGICAL PROCEDURE ON THE EXTENT OF THE RESULTING PARESIS

EXTENT OF SURGERY AND NUMBER OF PATIENTS	EXTENT OF RESULTING PARESIS (PER CENT)			
	LOWER LIP	LOWER AND UPPER LIPS	LIPS AND EYELIDS	LIPS, EYELIDS, AND FOREHEAD
Enucleation,* 8	38	--	--	--
Subtotal parotidectomy, 60	50	28	3	19
Total parotidectomy, 23	22	13	22	43
Total parotidectomy and neck dissection, 5	20	--	60	20

*Remaining lesions yielded no paresis.

NERVE EXPOSURE AND PARESIS

In analyzing the effect of the extent of exposure of the facial nerve, the cases were divided into four categories, as in Table IV. The first column includes only the cases in which no branch or only the mandibular branch of the nerve was exposed during surgery. The second column includes those cases in which all of the main stem and not over 2 cm. of the upper and 3 cm. of the lower main divisions were visualized in the surgical field. This extent of division exposure is characterized as minimal whereas a greater length of exposure of the main two divisions is designated as moderate. In the third column, the cases with the main trunk and one minimal and one moderate division exposure are considered. The fourth column includes all the cases in which the main stem and both main divisions are moderately or extensively exposed. In some instances this included an almost complete exposure of the entire facial nerve up to the point where the branches dipped deep to and into their corresponding facial muscles. A study of Table IV reveals that the extent of the resulting paresis is roughly directly proportional to the extent of exposure of the facial nerve.

TABLE IV. THE EFFECT OF THE EXTENT OF FACIAL NERVE EXPOSURE ON THE EXTENT OF THE RESULTING PARESIS

EXTENT OF EXPOSURE OF FACIAL NERVE AND NUMBER OF PATIENTS	EXTENT OF RESULTING PARESIS (PER CENT)			
	LOWER LIP	UPPER AND LOWER LIPS	LIPS AND EYELIDS	LIPS, EYELIDS, AND FOREHEAD
Mandibular branch or none, 9	44	0	0	0
Main trunk and both divisions, minimal, 9	89	0	0	11
Main trunk and one division, moderate, 38	54	35	5	16
Main trunk and both divisions, moderate or extensive, 40	25	22	12	41

Table V shows that the extent of exposure of the facial nerve is also directly proportional to the extensiveness of the surgical procedure.

Table VI reveals a direct correlation of increased facial nerve exposure with the eradication of lesions in the more dangerous nerve zones, such as in the preauricular and deep lobe regions.

On the basis of the data in Tables I to VI, it can be stated that the extent of postsurgical facial nerve paresis is, in a degree, directly proportional to the

extent of facial nerve exposure. The nerve exposure is greater in the more extensive surgery of the parotid salivary gland. Finally, lesions located in the deep lobe or in the preauricular area of the superficial lobe of the parotid gland require more extensive surgery, such as total parotidectomies which necessitate greater exposure of the facial nerve with its resulting more extensive facial nerve paresis.

TABLE V. THE EFFECT OF THE EXTENT OF THE SURGICAL PROCEDURE ON THE EXTENT OF EXPOSURE OF THE FACIAL NERVE

EXTENT OF SURGERY AND NUMBER OF PATIENTS	EXTENT OF EXPOSURE OF FACIAL NERVE (PER CENT)			
	MANDIBULAR BRANCH OR NONE	MAIN TRUNK AND BOTH DIVISIONS, MINIMAL	MAIN TRUNK AND ONE DIVISION, MODERATE	MAIN TRUNK AND BOTH DIVISIONS, MODERATE OR EXTENSIVE
Enucleation, 8	100	--	--	----
Subtotal parotidectomy, 60	1.5	15	63	20.5
Total parotidectomy, 23	----	--	--	100
Total parotidectomy and neck dissection, 5	----	--	--	100

TABLE VI. THE EFFECT OF THE LOCATION OF THE LESION ON THE EXTENT OF FACIAL NERVE EXPOSURE

LOCATION OF LESION AND NUMBER OF PATIENTS	EXTENT OF EXPOSURE OF FACIAL NERVE (PER CENT)			
	MANDIBULAR BRANCH OR NONE	MAIN TRUNK AND BOTH DIVISIONS, MINIMAL	MAIN TRUNK AND ONE DIVISION, MODERATE	MAIN TRUNK AND BOTH DIVISIONS, MODERATE OR EXTENSIVE
Lower pole (superficial lobe), 37	24	8	52	16
Pterygoid portion (superficial lobe), 23	—	26	38	36
Preauricular area (superficial lobe), 19	—	—	32	68
Deep lobe, 17	—	—	24	76

INFILTRATING LESIONS AND PARESIS

The cases were then considered from the standpoint of relationship of an infiltrating lesion with the extent of the postsurgical paresis (Table VII). This group of seventeen cases was compared with eighteen cases of encapsulated lesions in which there were intraparotid adhesions because of prior surgery and a third group of sixty-one cases of encapsulated lesions without prior surgery. Even though the infiltrating group had more of its lesions in the preauricular and deep lobe and had a higher percentage of total parotidectomies with more extensive facial nerve exposure, the resulting postoperative paresis was about equal in involvement with the other two groups. Apparently, then, infiltration as such does not add to the hazard of postoperative facial nerve paresis.

When the seven inflammatory lesions are analyzed, it is seen in Table VIII that the degree of paresis and the extent of paretic involvement are greater by almost 50 per cent than for the group as a whole. However, further study of

this group reveals that all the patients were treated by total parotidectomy with extensive nerve exposure. Therefore, the results can actually be ascribed to the extensive exposure of the facial nerve, whereas the inflammatory nature of the parotid gland lesion was responsible only in that it necessitated more radical surgery which resulted in more extensive nerve exposure.

TABLE VII. THE EFFECT OF AN INFILTRATING LESION ON THE EXTENT OF THE RESULTING PARESIS

COMPARATIVE FACTORS	ENCAPSULATED LESION WITH NO PRIOR TREATMENT	ENCAPSULATED LESION WITH PRIOR SURGERY	INFILTRATING LESION WITH OR WITHOUT PRIOR SURGERY
Number of patients	61	18	17
Per cent of total parotidectomies	20	33	66
Per cent of lesions in preauricular area and deep lobe	39	22	48
Per cent of all moderate to extensive exposure of facial nerve divisions	32	50	68
Extent of resulting paresis (per cent)			
Lower lip alone	13	50	35
Lower and upper lips	55	16	35
Lips and eyelids	8	11	6
Lips, eyelids, and forehead	24	23	24

TABLE VIII. THE EFFECT OF AN INFLAMMATORY LESION ON THE EXTENT AND DEGREE OF PARESIS AND THE RATE OF RECOVERY

EXTENT OF PARESIS AND NUMBER OF PATIENTS	DEGREE OF PARESIS		RECOVERY IN DAYS	
	INFLAMMATORY CASES	ALL CASES	INFLAMMATORY CASES	ALL CASES
Lower lip, 7	++++	+++	157	114
Upper lip, 5	+++	++	72	52
Eyelids, 4	+++	++	53	37
Forehead, 4	++++	++88	75	56

AGE AND PARESIS

The clinical impression that the older age group suffers more severe and more extensive facial nerve paresis is verified by a review of the data in Tables IX, X, and XI. The difference is particularly evident if the group from 10 to 39 years is compared with the 40- to 79-year group. After 40 years, the extensiveness of nerve paresis was over twice as great, in spite of the somewhat lesser extent of exposure of the facial nerve and less radical surgery; however, the tumors in the older age group were somewhat less favorably located. In the age group under 10 years there were only two patients, one 8 months and the other 5 years of age. Both had total parotidectomies for inflammatory and infiltrative lesions. Both developed extensive paresis but of mild degree with very rapid recovery in fourteen and fifty days, respectively. The inclusion of these two cases would have abnormally influenced the figures.

RECOVERY FROM PARESIS

In observing the progress of the paresis, it was noted that in about 50 per cent of the cases the maximum degree of involvement was noted two hours postoperatively while 75 per cent was evident by twenty-four hours and the

TABLE IX. THE PERCENTAGE OF EXTENSIVE SURGICAL PROCEDURES. EXTENSIVE NERVE EXPOSURE, AND DANGEROUSLY LOCATED LESIONS IN THE VARIOUS AGE GROUPS

AGE GROUP AND NUMBER OF PATIENTS	PER CENT OF TOTAL PAROTIDECTOMIES	GROUP AVERAGE (%)	PER CENT OF EXTENSIVE EXPOSURE OF FACIAL NERVE	GROUP AVERAGE (%)	PER CENT OF DEEP AND PREAURICULAR LOCATIONS	GROUP AVERAGE (%)
0 to 9, 2	100	—	100	—	100	—
10 to 19, 4	50	30	83	67	50	30
20 to 29, 12	25		65		25	
30 to 39, 14	21		64		28	
40 to 49, 19	26	26	59	62	32	40
50 to 59, 14	21		65		44	
60 to 69, 17	23		61		47	
70 to 79, 15	40		65		40	

TABLE X. THE EXTENT OF THE PARESIS AND THE RATE OF RECOVERY IN THE VARIOUS AGE GROUPS

AGE GROUP AND NUMBER OF PATIENTS	EXTENT OF PARESIS (PER CENT)					RECOVERY IN DAYS	
	LOWER LIP	BOTH LIPS	LIPS AND EYELIDS	LIPS, EYELIDS, AND FOREHEAD	GROUP AVERAGE	AVERAGE	GROUP AVERAGE
0 to 9, 2	—	—	50	50	—	32	—
10 to 19, 4	—	50	—	25	13	115	87
20 to 29, 12	50	16	16	8		40	
30 to 39, 14	35	43	8	14		120	
40 to 49, 19	42	16	5	32	28	117	125
50 to 59, 14	56	7	7	30		122	
60 to 69, 17	36	40	—	24		121	
70 to 79, 15	40	13	7	27		142	

TABLE XI. THE RELATIONSHIP OF AGE TO THE DEGREE OF PARESIS (+ TO ++++) AND RATE OF RECOVERY (IN DAYS)*

AGE GROUP	LOWER LIP		UPPER LIP		EYELIDS		FOREHEAD	
	DEGREE OF PARESIS	RECOVERY IN DAYS	DEGREE OF PARESIS	RECOVERY IN DAYS	DEGREE OF PARESIS	RECOVERY IN DAYS	DEGREE OF PARES'S	RECOVERY IN DAYS
0 to 9	+++	32	+ss	17	+	3	+++	30
10 to 19	++++	153	++	17	+	30	++++	90
20 to 29	++ss	42	++	20	+	15	++	12
30 to 39	+++	101	++	40	++ss	48	++++	85
40 to 49	++ss	118	++	56	+ss	31	++	35
50 to 59	+++	104	+++	85	++ss	40	+++	57
60 to 69	+++	135	++ss	47	+++	57	++	60
70 to 79	+++ss	164	+++	100	+++	63	+++	97
0 to 39	+++	79	++	29	+ss	25	++ss	40
40 to 79	+++	130	++ss	67	++ss	46	++ss	73

*Cases in which main stem was not exposed were excluded.

maximum in forty-eight hours. This method of paresis determination was particularly useful because a progressive paresis reassured the surgeon that the nerve had been traumatized rather than severed, since in the latter instance the maximum degree of paralysis would have been immediately evident. It was also noted that in those instances in which the paresis was observably progressive, the paresis appeared first in the lower lip, next in the upper lip, then in the forehead, and last in the eyelids. Recovery took place in the opposite sequence except for the forehead and upper lip (see Table XII). It was

also noted that the more extensive the involvement was, the longer it took for final recovery of each single patient (see Table XIII), and in almost all instances the lower lip was the last to recover (see Table XII). In Table XIV a direct relationship can be seen to exist between the days necessary for final recovery and the degree and extent of the paresis.

TABLE XII. THE RATE OF RECOVERY OF EACH PARETIC DIVISION CONSIDERED SEPARATELY AND WITHOUT REGARD TO THEIR COMBINED INVOLVEMENT

DIVISION INVOLVED IN PARESIS AND NUMBER OF PATIENTS	AVERAGE DEGREE OF PARESIS (+ to ++++)	DAYS BEFORE RECOVERY	
		RANGE	AVERAGE
Lower lip, 92	+++	1-365	114
Upper lip, 53	++	1-360	52
Eyelids, 30	++	1-150	37
Forehead, 23	++88	8-210	56

TABLE XIII. THE EFFECT OF THE EXTENT OF THE PARESIS ON THE RATE OF FINAL RECOVERY OF ALL OF THE INVOLVED DIVISIONS

EXTENT OF PARESIS (92 CASES) AND NUMBER OF PATIENTS	RECOVERY IN DAYS	
	RANGE	AVERAGE
Lower lip, 39	2-360	86
Lower and upper lips, 23	5-360	110
Lips and eyelids, 7	14-360	145
Lips, eyelids, and forehead, 23	15-365	161

TABLE XIV. THE EFFECT OF THE EXTENT AND DEGREE OF PARESIS ON THE AVERAGE RATE OF RECOVERY (IN DAYS) OF EACH DIVISION

EXTENT OF PARESIS AND NUMBER OF PATIENTS	DEGREE OF PARESIS			
	+	++	+++	++++
Lower lip only, 39				
(1) lower lip	4	56	85	165
Lower and upper lips, 23				
(1) lower lip	16	68	160	146
(2) upper lip	14*	45	7*	—
Lips and eyelids, 7				
(1) lower lip	14	82	72*	250
(2) upper lip	7	39	—	82
(3) eyelids	8	—	30*	—
Lips, eyelids, and forehead, 23				
(1) lower lip	—	55	137	180
(2) upper lip	30	40	53	137
(3) eyelids	9	60	72	78
(4) forehead	40	42	60	84

*One case only.

A review of the seventeen cases with infiltrating lesions revealed no special increase in the degree of paresis or in recovery time as compared to the other groups (see Table XV).

Age, on the other hand, seemed definitely to influence the recovery time, with the best results apparent in the younger groups. In Table IX it is shown that patients under 40 years had an average group recovery time of eighty-seven days, as against 125 days in the group over 40 years, in spite of the fact that the younger group had more extensive surgery and nerve exposure (see Table X). This is further emphasized in Table XI where it is revealed that

the recovery time was longer in the group over 40 years even though the degree of initial paresis was the same as or even less, in many instances, than in the group under 40 years.

TABLE XV. THE EFFECT OF AN INFILTRATING LESION OR PRIOR SURGERY ON RECOVERY FROM PARESIS

	ENCAPSULATED LESION WITH NO PRIOR TREATMENT		ENCAPSULATED LESION WITH PRIOR TREATMENT		INFILTRATING LESION WITH OR WITHOUT PRIOR TREATMENT	
AREA OF PARESIS	AVERAGE DEGREE OF PARESIS	RECOVERY IN DAYS	AVERAGE DEGREE OF PARESIS	RECOVERY IN DAYS	AVERAGE DEGREE OF PARESIS	RECOVERY IN DAYS
Lower lip	(58)* +++	111	(17)* +++	148	(17)* +++	90
Upper lip	(34) ++ss	51	(8) ++	83	(11) ++	42
Eyelids	(20) ++	41	(5) ++	32	(5) ++ss	44
Forehead	(15) ++ss	60	(3) +++	43	(4) +++	75

*Number of patients.

DISCUSSION

Various procedures were attempted in order to cut down on the degree and extent of the postoperative paresis. The nerve was traumatized as little as possible and was never raised out of its bed or elevated with hooks or suture material except where it was absolutely necessary in order to remove a deeply placed lesion. Electric stimulation for delineation of nerve fibers was never used. The exposed nerve was blotted with moist saline solution or blood-soaked sponges, which latter were often left to cover the nerve elements during the course of surgery. The impression was gained that such moist gauze contact was beneficial. It was also noted that in cases of deep lobe tumors, where the nerve was already markedly stretched and where a great deal of additional stretching and manipulation was necessary in order to free the tumor, no comparable increase in the extent of the paresis was noted. This was often very surprising, especially when much lesser manipulation of the normally positioned and nonstretched nerve resulted in complete and total paresis. It was concluded that a facial nerve which has been subjected to extensive progressive stretching by a tumor can withstand further marked manipulation much better than a nerve that has not been stretched in this manner. The more frequent and extensive involvement of the lower lip as well as the longer duration of its paresis is most likely due to the poor anastomotic connections of its mandibular branch with the other divisions of the facial nerve. In addition, the lower division with its mandibular branch is more often and more extensively exposed because of the presence of more lesions along its course and the necessity for exposing it in some degree regardless of the location of the lesion.

In no instance has any form of electrotherapy been used in the management of the paresis. The patients were instructed to execute all the facial muscular gestures actively, particularly with the teeth clamped closed and with effortful trials regardless of whether a response was noted or not. To

date, all patients have had complete return of facial nerve function in from one to 365 days. One patient has now gone one and one-half years with progressive improvement throughout that period but with about 25 per cent paresis of the lower lip still present. It is anticipated, based on the progress currently being made, that this patient will eventually get complete return of function. A two-year limit has been set before a case of paresis is considered to be permanent providing there has been no improvement in the previous three months. Often progress appears to be very slow over a period of months and then within a matter of several weeks complete restoration of function returns.

SUMMARY

Of 153 cases of parotid surgery, ninety-six were available for study of the resulting facial nerve paresis. The paresis was measured by one observer in order to eliminate differences in interpretation. A plus one (+) was noted for the mildest observable involvement and a plus four (++++) for what appeared to be maximum paresis. The extent of involvement was measured by dividing the paresis as it appeared in four regions, the lower lip, the upper lip, the eyelids, and the forehead. The degree and extent of the paresis were then correlated with the extent of exposure of the facial nerve, the radicalness of the surgery, the location of the lesion, the degree of infiltration of the lesion, and the age of the patient. Minimal exposure of a main division of the facial nerve was considered to be 2 cm. or less for the upper division and 3 cm. or less for the lower. More than that was classified as moderate or extensive exposure, and all cases with almost complete exposure of the facial nerve were included in the latter group. The main stem was exposed in all except six cases. The radical operations consisted of total parotidectomy with or without radical neck dissection, and next, in order of decreasing severity, were the subtotal parotidectomy and enucleation procedures. For simplicity's sake, the lesions were classified as being located either in the lower pole of the superficial lobe, in the pterygoid extension of this lobe, or in the preauricular position of the superficial lobe. The deep lobe lesions also included those of the isthmus and intraoral or parapharyngeal position. The diffuse lesions included not only the inflammatory lesions but also the infiltrating malignant neoplasms and cases recently subjected to excision or biopsy wherein the surgical bed was still in the process of healing by granulation tissue and cellular infiltrate. The age grouping was combined to compare those under 40 years of age with those over 40 years in order to eliminate the comparison of too small a number of patients, as would have been the case if the ten-year groupings had been used.

CONCLUSION

Some degree of paresis will appear in practically all cases of exposure of the facial nerve. This paresis is about 50 per cent complete in two hours, 75 per cent in twenty-four hours, and reaches its maximum in forty-eight hours.

The paresis usually appears first in the lower lip, then in the upper lip, forehead, and eyelids, and disappears, as a rule, in the opposite sequence. The lower lip is earlier, more often, and more severely involved.

The extent and degree of the paresis and the delay in recovery are in almost direct proportion to the extent of exposure of the facial nerve, which latter depends on the extent of the surgery, which, in turn, is most often related to the location of the lesion.

Everything else being more or less comparable, patients under 40 years of age have less paresis and recover more quickly than those over 40 years.

If no nerve has been severed, recovery in from one day to two years can be anticipated in all cases regardless of the severity of the paresis or the age of the patient.

Recovery from the paresis occurred in all cases without the aid of electrotherapy.

PROLONGED ANTICOAGULANT THERAPY WITH SUBCUTANEOUSLY ADMINISTERED CONCENTRATED AQUEOUS HEPARIN

HYMAN ENGELBERG, M.D., LOS ANGELES, CALIF.
WITH THE TECHNICAL ASSISTANCE OF MARIAN Z. BERK

WITHIN the past decade there has been growing recognition of the dangers of postoperative thromboembolic disease. Evidence has been presented indicating an actual increase in the occurrence of venous thrombosis.[1] The use of anticoagulant drugs prophylactically in those postoperative patients considered more likely to develop thromboembolic disease resulted in a marked reduction in its incidence.[2-5]

The search for an ideal anticoagulant continues, however, in recognition of the fact that present forms of therapy have defects. All orally effective preparations thus far available are toxic, may have delayed and unpredictable effects, and require prothrombin-time determinations almost daily for adequate safety.[6] Despite these precautions, however, occasionally serious bleeding occurs, at times at therapeutic prothrombin levels.[7-10] This is so because hemorrhage following these drugs is not entirely a measure of the degree of prothrombin deficiency, it may occur when this deficiency is not great,[10] and it is difficult to control. Thus coumarin drugs are dangerous to use unless excellent laboratory facilities are available, and at times even then. Heparin, on the other hand, has until now had the disadvantage of requiring intravenous injections every six hours or by constant drip, intramuscular injections every eight hours with occasional painful areas resulting, or the use of mixtures of heparin in retarding menstruums, which are frequently extremely painful and difficult to administer. However, the safety of heparin has been noted by all investigators. It is generally agreed that if heparin could be given easily, it would be the preferred anticoagulant.[3-14] It is a physiologic substance with a great margin of safety between the therapeutic dose and that producing spontaneous hemorrhage, it is effective, quick acting, easily controlled, may be used during pregnancy, is rapidly neutralized by the infusion of whole blood or by the injection of protamine sulfate,* and it has very few contraindications.[3, 5, 11] It also has a marked inhibitory effect on platelet agglutination,[15] it decreases blood viscosity,[16] it inhibits experimental pulmonary edema,[17] it may play a role in the normal formation of collagen,[18] and it alters serum lipoproteins in the direction of increased normality.[19] These are all important actions of heparin which do not occur following the use of other anticoagulants. Furthermore, there is good experimental evidence that when heparin is given in order to maintain steady anticoagulation, it is a much more effective preventative of vascular thrombosis than Dicumarol, unless the latter is given in doses large

Received for publication Jan. 18, 1954.

*Vitamin K or K_1 emulsion is used to counteract the anticoagulant action of drugs which act primarily on prothrombin production, but is not needed to neutralize the effect of heparin.

enough to depress the prothrombin time to levels generally considered dangerous.[20] Wessler,[21] who has studied intravascular coagulation in the isolated venous segment of dogs, found the anticoagulant effect of heparin superior to that of Dicumarol, and observed that bleeding occurred with Dicumarol when an adequate anticlotting effect was not yet present. He felt that substances such as Dicumarol, which depress that part of the coagulation sequence concerned with prothrombin conversion, may not provide as optimal an anticoagulant effect as heparin or heparin-like compounds which block fibrin deposition through other mechanisms.

Several authors have described the use of concentrated aqueous heparin. Stats and Neuhof,[13] using 100 mg. per cubic centimeter of aqueous heparin intramuscularly, obtained good anticoagulation in postsurgical cases in doses of 100 to 140 mg. every eight hours or 120 to 200 mg. every twelve hours. Baker, Warren, and Belko[14] successfully used 100 mg. per cubic centimeter of aqueous heparin intramuscularly in 40 to 50 mg. doses every four hours. Wymer, Goodwin, and Birbeck[22] administered concentrated aqueous heparin intramuscularly in doses of 150 mg. every twelve hours or 100 mg. every eight hours with good results. Recently, Artz and Amspacher[23] presented their findings with various types of heparin. They reported that 200 mg. per cubic centimeter of aqueous heparin given subcutaneously in 200 mg. doses gave good anticoagulation for twelve hours in all cases with a slow, variable drop toward preinjection levels at twenty-four hours. The results were as good as those obtained with a 200 mg. dose of heparin in gelatin, and with much less untoward reaction and discomfort than with the gelatin preparation.

This paper describes studies of the anticoagulant action of concentrated aqueous heparin* administered subcutaneously. All injections were given subcutaneously, not intramuscularly, about one to one and one-half inches below the posterior iliac crest. This area is preferred as it is a relatively painless one. The heparin was administered slowly using a No. 25 or No. 26 needle, thus minimizing capillary rupture and consequent ecchymosis.† The three-tube Lee-White tests were all identically run by the same technicians, using the end-point technique described by McCleery and Yarborough.[24] The last cubic centimeter of blood withdrawn was placed in Tube 3, the next blood in Tube 2, then in Tube 1, and the first 1 to 2 c.c. of blood withdrawn was discarded. Control levels ranged from ten to thirty-one minutes.

Table I presents data showing the duration of anticoagulant effect of various concentrations of subcutaneous aqueous heparin in twenty-five ambulatory patients in whom a trial of heparin therapy for severe atherosclerotic disease was being initiated. It is apparent that a dose of 200 mg., in concentration of either 200 mg. or 100 mg. per cubic centimeter, gave adequate anticoagulation for twenty-four hours in about one-half the cases. The more concentrated heparin was usually more prolonged in its effect. With increased dosage, there

*Supplied by Darwin Laboratories and Lederle Laboratories Division.

†It is desirable to demonstrate this technique to the nurse to guarantee that the injection is a subcutaneous one, not intramuscular.

TABLE I. LEE-WHITE COAGULATION TIMES* FOLLOWING SUBCUTANEOUS AQUEOUS HEPARIN IN VARYING CONCENTRATION AND DOSAGE: AMBULATORY PATIENTS

PATIENT	WEIGHT (POUNDS)	CONTROL TIME	COAGULATION TIMES 24 HOURS AFTER HEPARIN			
			200 MG. DOSE 200 MG./C.C.	200 MG. DOSE 100 MG./C.C.	250 MG. DOSE 200 MG./C.C.	300 MG. DOSE 200 MG./C.C.
1	175	17	18			81
2	152	21	95	22		
3	142	17	19	38	55	
4	141	17	26	27	43	
5	159	28	85	33		
6	126	25	37	31	83	
7	112	26	31	36	42	60
8	101	25	43			
9	180	23	30	15	51	
10	138	29	28	91		
11	176	31	38	41	50	64
12	151	25	52	57		
13	184	12	46			
14	143	20	56	20		
15	157	17	65	58		
16	152	18	44	60		
17	168	31	120	29		
18	131	27	54	33		74
19	164	27	102	77		
20	115	31	72	46		
21	149	30	47	65	71	
22	169	14	40			
23	163	10	39	19		
24	164	24	61			
25	168	11	16		24	29

*In minutes.

TABLE II. SERIAL COAGULATION TIMES* AFTER SUBCUTANEOUS AQUEOUS HEPARIN IN VARYING CONCENTRATION AND DOSAGE

PATIENT	DOSE AND CONCENTRATION (MG. IN C.C.)	CONTROL	½-1 HR.	4-6 HR.	16-20 HR.	24 HR.	40 HR.
1	200 in 1	17	59		32	19	
	200 in 2	19	62		59	38	
2	200 in 1	17	26	37		26	
	200 in 2	21	55	120		27	
	250 in 1¼	17	26	120		43	
3	200 in 1	28	90		82	85	31
	200 in 2	30	100		41	33	25
4	200 in 1	25	75	60	46	37	21
	200 in 2	23	95	70	38	31	19
	250 in 1¼	29	120	112	90	83	49
5	200 in 1	29		42		28	
	200 in 2	29		100		91	
6	200 in 1	23	36	46	41	30	20
	200 in 2	27	120	90	21	15	17
	250 in 1¼	24	45	77	73	51	28
7	200 in 1	25	78	62		52	
	200 in 2	23	56	90		57	
8	200 in 1	22	40	92		56	
	200 in 2	20	50	150		20	
9	200 in 1	26	56	61	50	31	28
	300 in 1½	24	58	76	60	60	41
10	200 in 1	24	56	60	64	61	24
11	200 in 1	25	41	58	50	43	31
12	200 in 1	15	28	40	32	22	
13	200 in 1	12	26	38	25	20	
14	300 in 1	17	30	52	58	55	28
15	300 in 1	11	18	75	60	40	20

*In minutes.

was increased duration of effect. A 300 mg. dose of the more concentrated material gave adequate anticoagulation in all five of the patients in whom it was administered. Mild stinging or minor ecchymosis occurred infrequently.

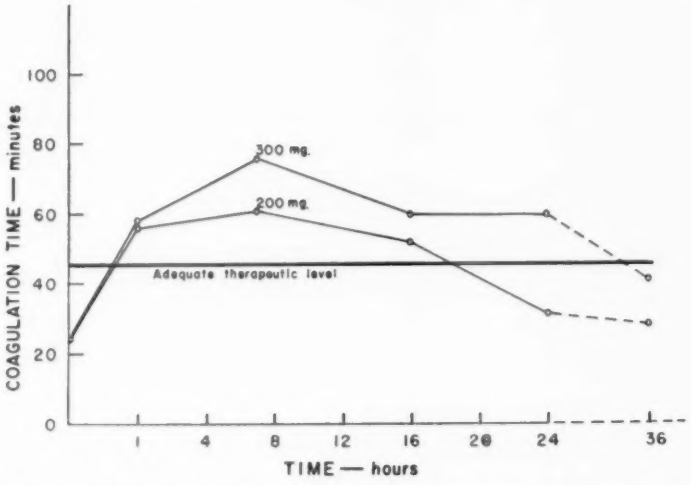


Fig. 1.—Coagulation times following different doses of heparin in the same patient.

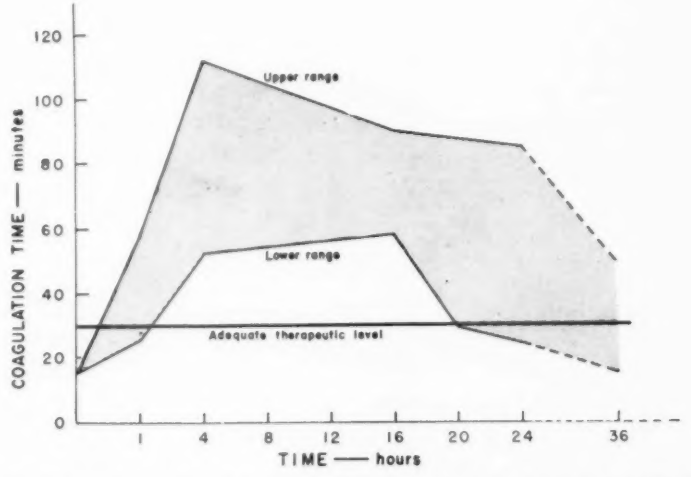


Fig. 2.—Coagulation times following a single 300 mg. dose of heparin subcutaneously. Composite figure of observations in fourteen patients.

Table II presents serial data on fifteen subjects. The anticoagulant activity usually begins within one-half to one hour, is at its height in four to six hours, and then slowly declines at a variable rate. In all cases, an increased dose of the more concentrated heparin gave more prolonged Lee-White times, and there was a greater duration of effect. No untoward reactions were noted. This is in agreement with other investigators who, using intravenous heparin, have repeatedly emphasized the safety of heparin and feel that high peaks of anticoagulant activity are more desirable.[3-5, 11]

Table III illustrates the coagulation times following various doses of highly concentrated aqueous heparin administered subcutaneously in eleven patients

TABLE III. SUBCUTANEOUS CONCENTRATED AQUEOUS HEPARIN 200 MG. PER CUBIC CENTIMETER COAGULATION TIMES* IN ELEVEN CASES OF PHLEBOTHROMBOSIS, THROMBOPHLEBITIS, AND CORONARY THROMBOSIS

PATIENT	CONTROL	DOSE† (MG.)	24 HR.	DOSE (MG.)	48 HR.	DOSE (MG.)	72 HR.	DOSE (MG.)	96 HR.	1 WK.	DOSE (MG.)	1½-2 WK.
1	12	200	26	200	16	300	49	250 every 24 hr.	34	40	250 every 24 hr.	29
2	9	200	17	250	19	300	29	300 every 24 hr.	43	66	250 every 24 hr.	26
3	10	300 (no IV heparin)	20	400	23	200 every 12 hr.	125	175 every 12 hr.	41	52	175 every 12 hr.	43
4	13	200	19	300	21	150 every 12 hr.	35	150 every 12 hr.	39	47	150 every 12 hr.	40
5	8	250	11	400	27	150 every 12 hr.	25	175 every 12 hr.	50	38	300 every 24 hr.	24
6	15	300	44	300	34	300	50	300 every 24 hr.		59	300 every 24 hr.	67
7	14	250	21	300	30	150 every 12 hr.	48	150 every 12 hr.		45	300 every 24 hr.	35
8	11	250	17	300	28	300	55	300 every 24 hr.	46	34	300 every 24 hr.	38
9	17	250	34	300	30	150 every 12 hr.	48	150 every 12 hr.	46	57	250 every 24 hr.	32
10	11	250	24	300	20	150 every 12 hr.	43	150 every 12 hr.		65	300 every 24 hr.	39
11	16	300	44	300	67	250	33	250 every 24 hr.	42		250 every 24 hr.	51

*Lee-White times determined prior to next scheduled injection. Time in minutes.
†In all cases 50 or 100 mg. of heparin was given intravenously initially. The first subcutaneous dose was administered one to two hours later.

with thrombotic disease. It is apparent that somewhat larger doses of heparin were initially required in this group than in the nonthrombotic ambulatory patients presented in Tables I and II, despite the fact that all patients received a 50 to 100 mg. dose of heparin intravenously at the start of therapy. With some exceptions, a 250 to 300 mg. dose of subcutaneous heparin gave adequate anticoagulation for the full twenty-four-hour period. When 125 to 150 mg. was injected every twelve hours, excellent anticoagulation was uniformly maintained in this group of patients. In a few cases, there seemed to be a slight cumulative effect which was of no consequence. There were no reactions other than a few minor ecchymoses at the site of injections.

Fig. 1 shows the anticoagulant effect of varying doses of subcutaneous aqueous heparin in the same individual in graphic form. Fig. 2 shows the range of anticoagulant action following a 300 mg. subcutaneous injection of 200 mg. per cubic centimeter of aqueous heparin. The data are based on observations in fourteen patients who received this dose of heparin.

DISCUSSION

The results obtained are in essential agreement with those of Artz and Amspacher,[23] and demonstrate that subcutaneously administered concentrated aqueous heparin is a safe, dependable form of heparin therapy. At least with the 200 mg. per cubic centimeter concentration, increased duration of effect is obtained by increasing the dose to 250 to 300 mg. When the dose is increased above 200 mg., using the 100 mg. per cubic centimeter concentration, more than a 2 c.c. injection volume is necessary, and pain and ecchymosis may occur. Furthermore, from observations in two cases not included in the tables, the absorption is irregular and not quite so prolonged. When thrombotic disease is present, there is apparently a hypercoagulable state present for a time, and somewhat larger doses are initially required for adequate anticoagulant action.[25] In these circumstances, 125 to 150 mg. every twelve hours subcutaneously is a more reliable form of therapy than a double dose once every twenty-four hours either in aqueous solution or in a gelatin menstruum. With hospitalized patients, a dose of heparin twice daily presents no problem. The anticoagulant effect of subcutaneous heparin every twelve hours is so uniformly adequate and stable that repeated coagulation time tests are superfluous. In general, heavier patients require the larger dose. When patients are at home, a 300 mg. dose of 200 mg. per cubic centimeter of aqueous heparin given subcutaneously once daily will give good anticoagulation in most cases. This is as effective and as prolonged an anticoagulation as is usually obtained following single injections of heparin in retarding media.[26] Apparently, intramuscular injections of highly concentrated aqueous material are somewhat more rapidly absorbed than subcutaneous ones.[23, 27]

It is important to re-emphasize the wide margin of safety in the use of heparin as opposed to other anticoagulants. Hemorrhage due to heparin therapy is rare, and is easily counteracted by protamine sulfate intravenously or by blood transfusion. Bauer[5] has reported on over 400 postoperative patients

treated with large doses of heparin without serious bleeding. In view of its safety, and since the generally accepted therapeutically desirable range of two to four times the control coagulation time has few data to support it, many investigators[5, 11, 28] believe that the coagulation time can be prolonged to one to two hours with little danger. In this study no hemorrhages occurred despite frequent markedly prolonged Lee-White times. As one's experience in the use of heparin increases, there is less fear of hemorrhage and an increasing tendency to use larger doses, since these may facilitate recanalization and clot reabsorption.[9, 15, 26]

The question of the need for frequent Lee-White times is worthy of discussion. Although a control coagulation time determination is desirable, it is not mandatory since it reflects the altered coagulability of the blood which is often found during acute thrombotic disease, and since there is a wide therapeutic range with heparin in contrast to the narrow range of the coumarin drugs. Once an adequate dose has been set, and this can be done with one to two coagulation-time determinations, further tests are not required.[5] The few Lee-White times are desirable to ensure good anticoagulation, rather than to maintain "safe" levels. In view of this, the actual saving to the patient with oral anticoagulants as compared to heparin therapy is very little since with the former drugs very frequent prothrombin-time determinations are necessary, and these are notoriously unreliable except in experienced hands. Jorpes[4] and Bauer,[5] using intravenous heparin, did not use clotting time tests at all except in patients with impaired renal function.

Theoretically, apart from its efficacy and safety as an anticoagulant, the other known actions of heparin contribute to making it the drug of choice in the prevention and treatment of thromboembolic disease. Recently, it has been conclusively demonstrated that heparin lowers blood viscosity, that this occurs within a few seconds if it is given intravenously, and that the alteration in viscosity persists longer than the decrease in coagulation time.[16] In 1942, H. P. Wright[30] found that there was an increased adhesiveness of platelets following parturition and surgical operations, thus predisposing to thrombosis. Increased platelet adhesiveness was further investigated by Moolten and associates,[15] who found that it occurs regularly following surgery, trauma, especially fracture, arterial occlusion, cancer, and myocardial or pulmonary infarction. Heparin, in doses of 100 mg. intravenously or subcutaneously, promptly lowered platelet adhesiveness, whereas Dicumarol was ineffective despite good hypoprothrombinemia. Morrione[18] found that collagen fibers formed from amorphous soluble collagen only when heparin was added. In 1951, Graham and co-workers[19] reported that an injection of heparin results in a shift of serum lipoproteins in the direction of increased normality. These multiple beneficial effects are not possessed by the oral anticoagulants.

SUMMARY

1. Concentrated aqueous heparin (200 mg. or 100 mg. per cubic centimeter) administered subcutaneously uniformly affords excellent anticoagulation in doses of 125 to 150 mg. every twelve hours.

2. In the 200 mg. per cubic centimeter concentration, subcutaneous doses of 250 to 300 mg. administered once every twenty-four hours are usually adequate.

3. Aqueous heparin is easy to administer and causes few painful reactions.

4. Heparin is much safer, requires less laboratory control, and is easier to neutralize quickly than the oral anticoagulants thus far introduced.

5. Other actions of heparin have been discussed which are also beneficial, which are not possessed by the oral anticoagulants, and which contribute to making heparin the anticoagulant of choice.

REFERENCES

1. Ochsner, A., DeBakey, M. D., DeCamp, P. T., and da Rocha, E.: Thromboembolism; an Analysis of the Cases at Charity Hospital in New Orleans Over a 12-year Period, Ann. Surg. **134**: 405, 1951.
2. Mitch, E., Berman, L., and Egan, R.: Use of Bishydroxycoumarin (Dicumarol) for Prevention of Postoperative Thromboembolism, Arch. Surg. **67**: 142, 1953.
3. Bauer, G.: Heparin Therapy in Acute Deep Venous Thrombosis, J. A. M. A. **131**: 196, 1946.
4. Jorpes, J. E.: The Origin and the Physiology of Heparin; the Specific Therapy in Thrombosis, Ann. Int. Med. **27**: 361, 1947.
5. Bauer, G.: Nine Years' Experience With Heparin in Acute Venous Thrombosis, Angiology **1**: 161, 1950.
6. Wright, I.: The Pathogenesis and Treatment of Thrombosis, New York, 1952, Grune & Stratton, Inc.
7. London, R. E.: Dicumarol Fatality in Severe Hypertensive and Arteriosclerotic Cardiovascular Disease Despite Controlled Therapeutic Level, Circulation **1**: 205, 1950.
8. Berman, H., and Mainella, F. S.: Toxic Results of Anticoagulant Therapy, New York State J. Med. **52**: 725, 1952.
9. Martorell, F.: Dicumarol; Dangerous and Rather Ineffective Drug, Angiology **3**: 185, 1952.
10. Hogben, C. A. M.: The Relationship Between Prothrombin Time and Bleeding in the Clinical Use of Dicumarol After Operation, Circulation **2**: 369, 1950.
11. D'Alessandro, A. J.: Venous Thrombosis. The Problem and Its Management, Am. J. Surg. **85**: 652, 1953.
12. Brown, A.: Anticoagulants and Anticoagulant Therapy: a Review, Glasgow M. J. **33**: 225, 1952.
13. Stats, D., and Neuhof, H.: Concentrated Aqueous Heparin. A New Form of Intramuscular Administration, Am. J. M. Sc. **214**: 159, 1947.
14. Baker, D. V., Jr., Warren, R., and Belko, J. S.: The Deep Subcutaneous Administration of Concentrated Heparin, New England J. Med. **244**: 436, 1951.
15. Moolten, S. E., Vroman, L., and Vroman, G. M. S.: Adhesiveness of Blood Platelets in Thromboembolism and Hemorrhagic Disorders, Am. J. Clin. Path. **19**: 814, 1949.
16. Hurwitz, A., Yesner, R., and Cooke, R. W.: Ultrasonic Measurements of the Effects of Heparin on Blood Viscosity, Laboratory Investigation **1**: 436, 1952.
17. Luisada, A. A., and Contro, S.: Experimental Pulmonary Edema Following Rapid Carotid Infusion: Mechanism and Therapy, Circ. Research **1**: 179, 1953.
18. Morrione, T. J.: The Formation of Collagen Fibers by the Action of Heparin on Soluble Collagen: an Electron Microscope Study, J. Exper. Med. **96**: 107, 1952.
19. Graham, D. M., Lyon, T. P., Gofman, J. W., Jones, H. B., Yankley, A., Simonton, J., and White, S.: Blood Lipids and Human Atherosclerosis. II. The Influence of Heparin Upon Lipoprotein Metabolism, Circulation **4**: 666, 1951.
20. Kiesewetter, W. B., and Shumaker, H. B., Jr.: An Experimental Study of the Comparative Efficacy of Heparin and Dicumarol in the Prevention of Arterial and Venous Thrombosis, Surg., Gynec. & Obst. **86**: 689, 1948.
21. Wessler, S.: Studies in Intravascular Coagulation II. A Comparison of the Effect of Dicumarol and Heparin on Clot Formation in Isolated Venous Segments, J. Clin. Investigation **32**: 650-654, 1953.
22. Wymer, A., Goodwin, J. F., and Birbeck, A.: Prolonged Anticoagulant Therapy With Heparin, Brit. M. J. 893, 1952.
23. Artz, C. P., and Amspacher, W. H.: Evaluation of Various Methods of Administration of Heparin. Proc. Surg. Forum, Clin. Congress Am. Coll. Surgeons, Philadelphia, 1952, W. B. Saunders Company.

24. McCleery, R. S., and Yarborough, J. A.: A New Tolerance Test as a Guide to Clinical Heparin Therapy, Circulation **4**: 394, 1951.
25. Beaumont, J. L., Chevalier, H., and Lenegre, J.: Studies on Spontaneous Variations in Blood Coagulability Immediately Following Myocardial Infarction, Am. Heart J. **45**: 756, 1953.
26. Glueck, H. L., Podore, C. J., and Levinson, J. E.: Efficiency of Heparin in Retarding Media on the Maintenance of a Decreased Coagulability of the Blood, Circulation **2**: 530, 1950.
27. Field, J.: Personal Communication.
28. Neuhof, H.: Venous Thrombosis and Pulmonary Embolism, New York, 1948, Grune & Stratton, Inc.
29. Friedman, I. A., Schwartz, S. O., and Vincenti, M.: Survey of Clotting Tests for Coagulation Profile in Normal and Diseased Persons, J. A. M. A. **150**: 83, 1952.
30. Wright, H. P.: Changes in the Adhesiveness of Blood Platelets Following Parturition and Surgical Operation, J. Path. & Bact. **54**: 461, 1942.

VEINS AFTER SYMPATHECTOMY

PETER BEACONSFIELD, M.D., LONDON, ENGLAND

(From the Department of Surgery, Postgraduate Medical School of London)

INTRODUCTION AND PLAN OF INVESTIGATION

WHENEVER blood flow through a sympathectomized limb is described or discussed, it is in fact the blood flow through the arteries which is referred to. It is, therefore, of considerable interest to examine the part played by the veins after sympathectomy. The importance of the state of the veins in the maintenance of the normal peripheral circulation is well established, particularly as the greater part of the total blood volume lies within them (McDowall, 1935; Landis and Hortenstine, 1950). After sympathectomy, do they behave passively, merely dilating as a result of the increased blood flow through the part, or are they in fact capable of independent vasodilation irrespective of whether the blood flow through that part is increased or not?

The number of patients suffering from diseases of the veins is infinitely greater than those suffering from arterial affections, and sympathectomy is sometimes carried out for venous disorders, particularly where venous drainage is impaired. It should not be forgotten that the innervation of the veins is the same as that of the arteries, and some investigators claim that they are more sensitive to stimuli than the arteries (Kuntz, 1934; Franklin, 1937; de Sousa Pereira, 1946).

It was Lewis and Landis (1929) who first noticed that after sympathectomy the veins of the affected area were distended for a variable period of time. This time taken for the recovery of vasomotor tone in veins is of considerable importance, and to try to obtain a fairly accurate estimate of its duration, an investigation by infrared photography was undertaken. Infrared photography was first used in medicine by Professor Haxthausen of Copenhagen in 1933, and demonstrated with a fair degree of accuracy the size and number of the larger superficial veins in the area.

Infrared photographs were taken of the palmar surfaces of the hand and forearm in four patients before and forty-eight hours, three months, and twelve months after cervicodorsal sympathectomy. Blood flows through the hand and forearm were measured at the same time to record the skin and muscle blood (arterial) flow. The size of the hand was measured before and at the same intervals after sympathectomy by Archimedes' principle, a demarcation line at the wrist being carefully drawn to ensure immersion of the part to the same level each time. Indirect heating tests were performed before and at two weeks, two months, and twelve months after the operation to verify the completion of the sympathectomy. At the end of each indirect

Received for publication, Feb. 23, 1954.

heating test, the heating ratio (Barcroft and Hamilton, 1948) was calculated by the formula:

$$\text{H.R.} = \frac{\text{Blood flow before indirect heating}}{\text{Blood flow after indirect heating}}.$$

Before sympathectomy this ratio is 5 or more; after sympathectomy it should be 1 if the sympathectomy is complete.

Each experiment was carried out under standard laboratory conditions.

RESULTS

The readings of the hand and forearm blood flows are tabulated in Table I. The mean of the four patients investigated was 3.1 ml. per 100 ml. of tissue per minute and 2.3 ml. before operation, respectively. Forty-eight hours after sympathectomy, the blood flow was 24.3 ml. in the hand and 10.0 ml. in the forearm. Three months after sympathectomy, the mean blood flow was the same as the flow before the operation.

TABLE I. HAND BLOOD FLOW (MILLILITERS PER 100 ML. OF TISSUE PER MINUTE)

CASE NO.	BEFORE SYMPATHECTOMY	24 HR. AFTER SYMPATHECTOMY	3 MO. AFTER SYMPATHECTOMY	12 MO. AFTER SYMPATHECTOMY
1	3.8	28.3	3.1	2.9
2	1.7	23.1	2.2	2.7
3	2.7	19.7	3.3	3.1
4	4.1	26.3	3.7	4.0
Mean	3.1	24.3	3.1	3.2
		Forearm Blood Flow		
1	2.7	8.3	1.2	1.7
2	1.5	5.3	2.3	2.1
3	3.0	14.1	1.9	2.7
4	1.9	12.3	2.7	1.7
Mean	2.3	10.0	2.2	2.0

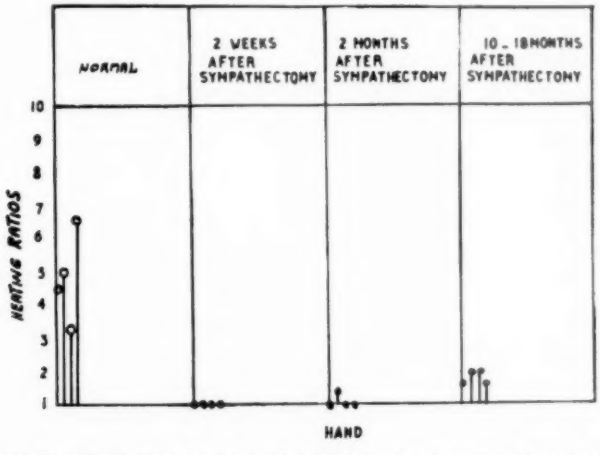


Fig. 1.—Response to vasomotor tests performed on four upper limbs after sympathectomy, arranged from left to right in order of time interval between operation and testing. Vasomotor reflexes were present in the limbs tested twelve months after operation.

The heating ratio two weeks after sympathectomy was 1 in all four patients, while at twelve months there was an increase in hand blood flow after indirect heating in all instances (Fig. 1).

The hand volume increased after sympathectomy (Table II) and was still increased three months later although the arterial blood flow had returned to normal, but at twelve months after sympathectomy the volume had regained its preoperative measurement. The increase in hand volume forty-eight hours after sympathectomy proves to be statistically significant ($P < 0.01$).

TABLE II. HAND VOLUME (IN CUBIC CENTIMETERS)

CASE NO.	BEFORE SYMPATHECTOMY	48 HR. AFTER SYMPATHECTOMY	DIFFERENCE	3 MO. AFTER SYMPATHECTOMY	12 MO. AFTER SYMPATHECTOMY
1	390	485	95	460	425
2	480	595	115	500	505
3	475	586	111	525	492
4	505	565	60	520	510
Mean	462	557*		501	485
		($P < 0.01$)			

*Significant difference.

Photographs of one of the patients are reproduced here to illustrate the results (the results in all four were similar).

Patient No. 1, a 35-year-old woman, was suffering from marked Raynaud's phenomenon. The hand and forearm blood flows in this case had returned to the preoperative level three months after sympathectomy, but the infrared photograph taken at the same time showed that the network of veins, which increased considerably in size and number forty-eight hours after operation, was still considerably larger than in the preoperative photograph. The hand volume, which increased after sympathectomy, was still elevated after three months but returned to the preoperative level twelve months after the operation. The infrared photograph taken twelve months after operation still reveals the veins to be more prominent than before the operation (Fig. 2).

TABLE III. FOOT VOLUME (IN CUBIC CENTIMETERS)

CASE NO.	BEFORE SYMPATHECTOMY	48 HR. AFTER SYMPATHECTOMY	DIFFERENCE	3 MO. AFTER SYMPATHECTOMY	12 MO. AFTER SYMPATHECTOMY
1	750	996	246	820	805
2	1,000	1,230	230	1,100	1,000
3	980	1,200	220	1,000	1,020
4	850	1,126	276	1,050	974
5	975	1,150	175	1,025	1,000
6	785	975	190	836	823
Mean	890	1,113*		972	937
		($P < 0.01$)			

*Significant difference.

TABLE IV. FOOT BLOOD FLOW (MILLILITERS PER 100 ML. OF TISSUE PER MINUTE)

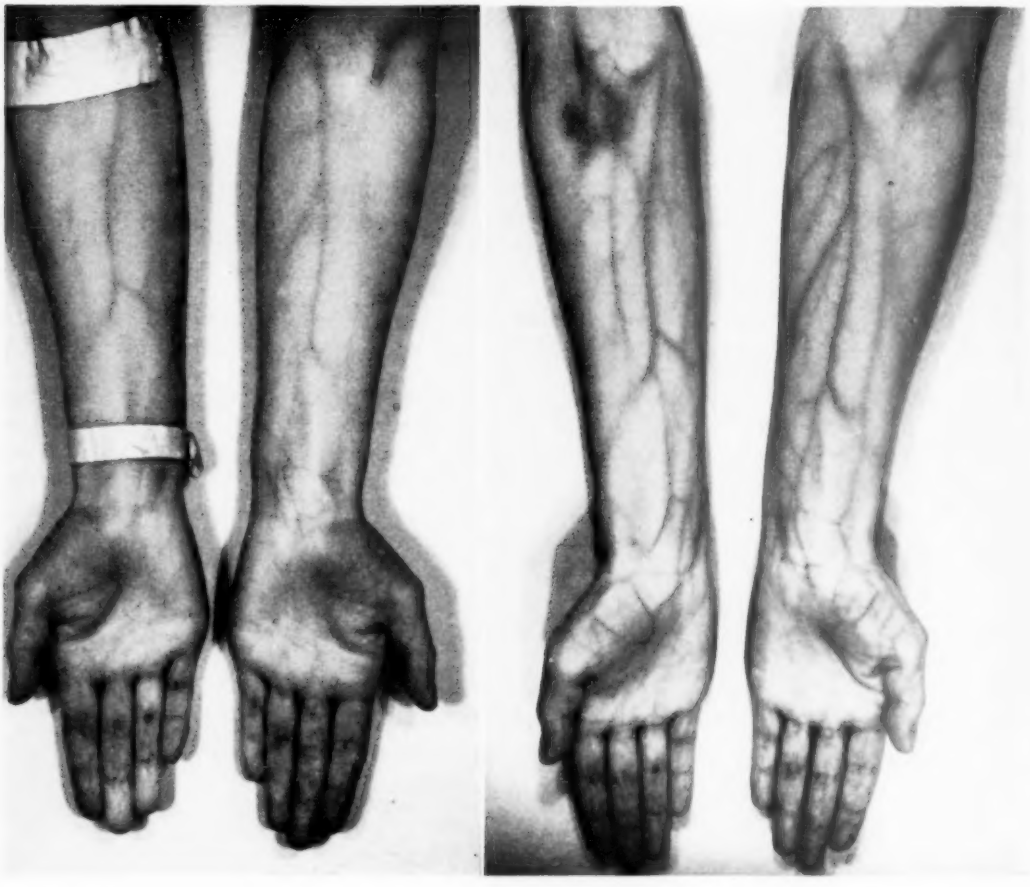
1	1.7	10.3	2.3	2.7
2	1.5	6.1	2.0	1.8
3	2.4	9.0	2.7	2.3
4	1.9	11.0	2.0	2.0
5	0.8	5.0	1.3	0.9
6	1.3	1.9	1.1	1.3
Mean	1.6	7.2	1.9	1.8

COMMENTS

Veins dilate after sympathectomy. The vasomotor tone begins to return to preoperative level shortly after sympathectomy but does not reach this

level for at least twelve months, which is a considerably longer period than is the case with arteries of the same limb.

The blood flow through the hand and forearm returns nearly to the preoperative level by the end of the second week, and by three months has returned to the presympathectomy level.



A. *B.*

Fig. 2.—Infrared photographs of patient No. 1. *A*, Before sympathectomy. *B*, Forty-eight hours after cervicodorsal sympathectomy (both sides). *C*, Three months after sympathectomy. *D*, Twelve months after sympathectomy.

Attempts to investigate the lower limbs by infrared photography were not successful because there are no networks of superficial veins below the knee except on the dorsum of the foot, and the situation does not, therefore, lend itself to this particular investigation. However, the foot volume and foot blood flows were measured in six subjects (Tables III and IV), and from the tables it can be seen that the results vary little from those recorded for the hand. In one subject (No. 6) suffering from advanced arteriosclerosis, there was no actual increase in foot blood flow, but the foot volume was increased, and on examination of the foot some of the veins were obviously more prominent. The toe skin temperature in this patient increased from 21.5° C. before sympathectomy to 27.5° C. three months after the operation.

Neither infrared photography nor clinical observation is sufficiently exact to establish definite physiologic facts but, nonetheless, analysis of the foregoing results allows one to say with reasonable accuracy that the dilatation of veins after sympathectomy is not merely due to increased blood flow because of the arterial dilatation, but is in fact an active process since it occurs even when blood flow through the part is not increased. With this information in mind, I would like to venture a step further and suggest that the discrepancy which exists after sympathectomy between the blood flow and skin

C. *D.*

Fig. 2, *C* and *D*. *(For legend, see opposite page.)*

temperature in the denervated area (skin temperature after sympathectomy remains considerably higher than the preoperative level for an indefinite period of time, contrary to the blood flow, which returns to almost the preoperative level a few weeks after sympathectomy) is perhaps in part the result of the decreased venous tone after sympathectomy. The veins, having less smooth muscle fibers than the arteries, may not recover their vasomotor tone as readily as arteries after sympathectomy, thus allowing a larger quantity of blood being present in the limb after sympathectomy without there actually being an increase in blood flow per unit of time.

SUMMARY

An investigation to determine the venous vasomotor tone after sympathectomy is described.

The return of preoperative vasomotor tone in veins takes more than twelve months from the time of sympathectomy and is not necessarily related to arterial vasodilatation and increased blood flow.

The delay in the return of the preoperative vasomotor tone in veins is discussed in reference to prolonged elevation of skin temperature after sympathectomy.

REFERENCES

1. Barcroft, H., and Hamilton, G. T. C.: Results of Sympathectomy of the Upper Limb, Lancet **1:** 441, 1948.
2. Franklin, K. J.: A Monograph on Veins, London, 1937, Baillière, Tindall & Cox.
3. Haxthausen, H.: Infra-red Photography of Subcutaneous Veins: Demonstration of Concealed Varices in Ulcer and Eczema of the Leg, Brit. J. Dermat. **45:** 506, 1933.
4. Kuntz, A.: The Autonomic Nervous System, Philadelphia, 1934, Lea & Febiger.
5. Landis, E. M., and Hortenstine, J. C.: Functional Significance of Venous Blood Pressure, Physiol. Rev. **30:** 1, 1950.
6. Lewis, T., and Landis, E. M.: Some Physiological Effects of Sympathetic Ganglionectomy in the Human Being and Its Effect in a Case of Raynaud's Malady, Heart **15:** 151, 1929.
7. McDowall, R. J. S.: The Nervous Control of the Blood Vessels, Physiol. Rev. **15:** 98, 1935.
8. de Sousa Pereira, A.: The Innervation of the Veins. Its Role in Pain, Venospasm, and Collateral Circulation, SURGERY **19:** 731, 1946.

AN APPARATUS FOR AUTOMATIC INTRODUCTION OF RADIOPAQUE MEDIA IN TRANSLUMBAR AORTOGRAPHY

MARTIN LANGSAM, M.D., AND NATHAN D. WILENSKY, M.D., BROOKLYN, N. Y.

(From the Peripheral Vascular Service of the Jewish Sanitarium and Hospital for Chronic Diseases)

INTEREST in translumbar aortography has been stimulated in the past few years by the brilliant surgical approaches both here and abroad in the treatment of obstructive vascular lesions. Many workers, such as Leriche,[1] dos Santos, and in this country Wylie,[2] Julian, de Takats, and Dye,[3] and DeWolfe and associates,[4] have utilized translumbar aortography in the recognition and treatment of stenoses of major arteries.

Our own technique has been the same as that utilized by Wylie,[2] that is, the use of two needles introduced by the translumbar route with the rapid injection of 50 c.c. of Urokon after a scout film has been taken.

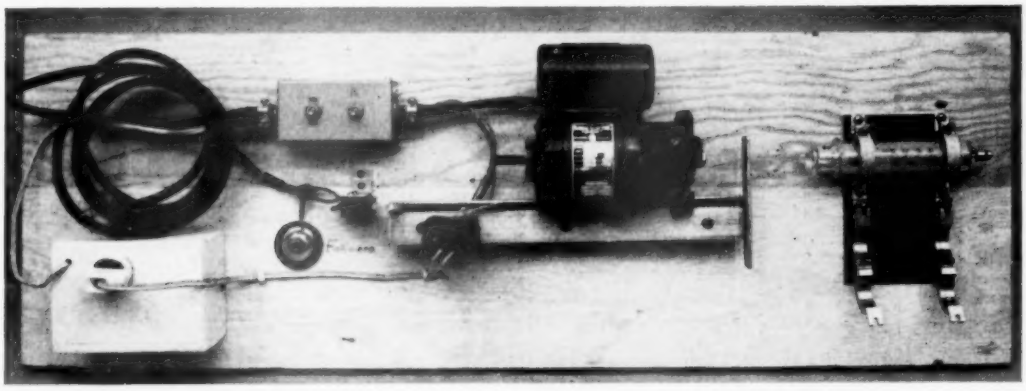


Fig. 1.—Apparatus for automatic introduction of a radiopaque media in translumbar aortography.

The need for an automatic injecting apparatus became apparent early in the course of our work for the following reasons:

1. The objections by the operator and the resident staff to repeated exposures to x-rays.

2. The inability to empty simultaneously both syringes. At times 7 to 10 c.c. of the radiopaque media remained in one syringe.

3. The repeated failure to inject all the radiopaque media within ten seconds and its consequent dilution and diminished opacification of the blood vessels.

4. The annoying incidents of sticking syringes and catching gloves.

5. The failure of the technician to take the x-ray film fast enough.

These objections led us to develop an apparatus which would inject the radiopaque media automatically and signal the x-ray technician when to take the x-ray films (the apparatus can be so wired as to eliminate the technician

Received for publication Feb. 5, 1954.

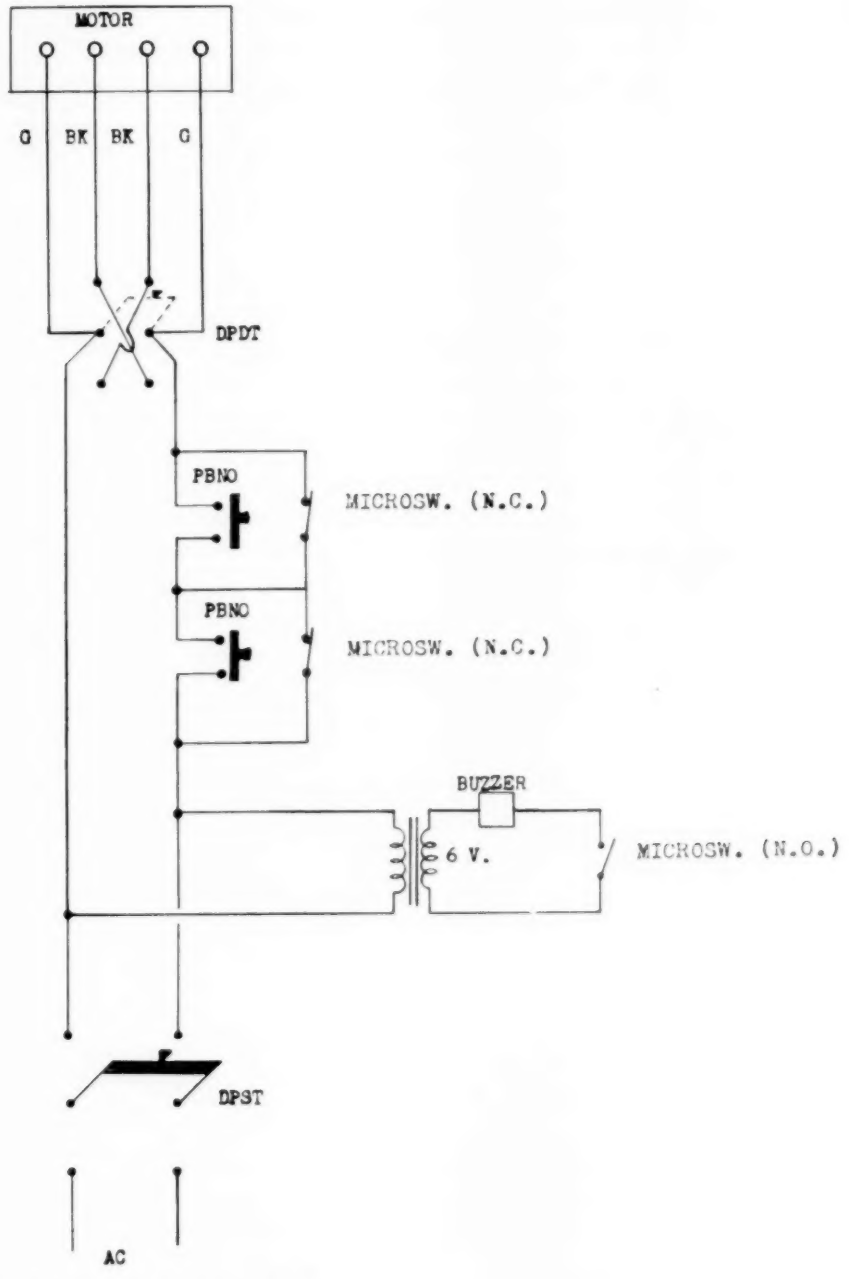


Fig. 2.—Electrical wiring diagram.
G—Green wire
BK—Black wire
DPDT—Double-pole, Double-throw switch
PBNO—Push button normally open
DPST—Double-pole, Single-throw switch
Microsw. (N.C.)—Microswitch normally closed
Microsw. (N.O.)—Microswitch normally opened

entirely). Previous authors[5, 6] have utilized the principle of hydraulic pressure to drive the plungers of the syringe. It was decided to develop an apparatus that depended on a motor-driven plate. The previous hydraulic machines were too cumbersome and difficult to adjust.

Following is a description of the apparatus that was developed after many failures:

The power is supplied by a Bodine capacitor motor with a built-in speed reducer. It runs on 115 volts, 60 cycles, and draws 0.14 amperes. The rated horsepower is 0.032 and is reduced to 5 r.p.m. Adjacent to the motor is a ½ inch thick brass plate with a channel cut into it, to permit a rack gear to run. The rack gear is ¼ inch by ¼ inch and is driven by a spur gear, which is attached to the drive shaft of the motor. To one end of the rack gear is braised a ⅛ inch brass plate so mounted that as it advances, it drives the plunger of the syringe.

The syringes must be mounted very securely; otherwise the force of the drive will lift them up and out of their holders. To avoid this, two pairs of brass holding rings, each with a hinged collar secured with a neck screw, were mounted onto a ¼ inch aluminum plate. This plate in turn is very firmly screwed down to the board.

There are two microswitches mounted on the channel plate. These are activated by a stud soldered into the rear of the rack gear. The top switch activates the buzzer (or can activate the x-ray machine) which, with its transformer, is mounted in the box.

The switching box contains an On and Off switch as well as a Forward and Reverse switch. It was necessary to put a starter button in the switch box because we had used two or three microswitches in relays to inject different quantities of radiopaque media, depending on what part of the vascular tree was to be visualized. In Figs. 1 and 2 the additional microswitches have been eliminated to avoid confusion.

After the injection is completed, the reverse switch is thrown, and the return drive is activated by the button in the switch box. The drive returns until the rearmost microswitch stops the motor. The rear microswitch is very important because if the drive is not stopped in time, it will tear the motor from its moorings. To restart the motor, there is a separate button which cuts out the effect of the rear microswitch.

SUMMARY

A new apparatus for automatic injection of radiopaque media in translumbar aortography is presented.

This apparatus is completely automatic and can be easily adjustable to inject different quantities of radiopaque material.

Acknowledgment.—We gratefully acknowledge the assistance of Isadore Lieberman and Ted Ross in building this piece of apparatus. Also we wish to thank Dr. A. Lewitan and Dr. Arthur Stern for their suggestions.

REFERENCES

1. Leriche, R., and Kunlin, J.: Essais de désobstruction des artéres thrombosées suivant la technique de Jean Cid dos Santos, Lyon chir. **42**: 675, 1947.
2. Wylie, E. J., and McGuinness, J. S.: Recognition and Treatment of Arteriosclerotic Stenosis of Major Arteries, Surg., Gynec. & Obst. **97**: 425, 1953.
3. Julian, O. C., de Takats, G., and Dye, W. S.: Segmental Nature of Peripheral Arteriosclerosis: Surgical Application, Angiology **4**: 12, 1953.
4. DeWolfe, V. G., et al.: Intermittent Claudication of the Hip and the Syndrome of Chronic Aorto-Iliac Thrombosis, Circulation **9**: 1, 1954.
5. Doss, A. K.: Translumbar Arteriography: An Apparatus for Injecting the Radio-Opaque Media, SURGERY **16**: 422, 1944.
6. Rosenman, L. D., Pearl, F. L., and Calvert, C.: A New Injection Device for Angiography, SURGERY **31**: 200-203, 1952.

A NEW AORTA CLAMP

EDWIN J. WYLIE, M.D., SAN FRANCISCO, CALIF.

(From the Department of Surgery, University of California School of Medicine)

TEMPORARY occlusion of the abdominal aorta is necessary in many of the surgical procedures used for the operative treatment of arteriosclerotic aneurysm or thrombosis of the abdominal aorta. The application of a clamp on the aorta, when there is arteriosclerotic disease present, may result in complications which are not seen in the occlusion of a normal aorta. The rigid and often calcified intima may be fractured by the sharp edges of many instruments currently in use and thereby lead to thrombosis when the clamp is released. A new aorta clamp has been designed to minimize this danger, and additional features have been incorporated to facilitate its use. The shape and construction of this clamp are illustrated in Fig. 1.

The opposing surfaces of the blades are wide and convex to graduate the arterial distortion over a greater distance. The resulting compression is analogous to that produced by occlusion of the aorta between two fingers. The upper blade is fitted with two rows of fine teeth to prevent the clamp from being moved distally by the proximal arterial pulse. The lower blade is smooth and rubber shod, so that it can be easily passed beneath the aorta. In cases of aorta thrombosis or aneurysm beginning just distal to the renal arteries, it is desirable to preserve the patency of these vessels. The proximal convexity of the blades has been useful for this purpose in that it allows adequate space to incise the aorta to within 1 or 2 cm. of this level. The length of the blades ($3\frac{1}{2}$ cm.) has been found adequate for complete occlusion of the normal-sized adult aorta (Fig. 2).

In procedures on the abdominal aorta, it is usually necessary to mobilize the intestines and to retract them superiorly on the chest wall. The handle of a clamp applied to the aorta proximal to the level of the inferior mesenteric arteries will often be angulated distally by the inadvertent pressure of the retractors or the assistant's hand, thereby distorting the aorta. The handle of the clamp is detachable to obviate this problem. It has been the practice to detach the handle once the clamp is in place and to reattach it when the clamp is opened.

Gross and microscopic observations of the arterial wall at the site of the application of the clamp have been made. Microscopic sections of the aorta were made at the clamped level in five dogs upon which experimental operations on the aorta had been performed. In all cases, the clamp had been in place for over one hour. The animals were sacrificed at intervals varying from twenty-four hours to three months. There was no evidence of inflammation,

Received for publication Feb. 8, 1954.

fibrosis, or intimal damage in any case. The clamp has been used for occlusion of the aorta in forty-six cases of thromboendarterectomy performed for arteriosclerotic thrombosis of the aorta or iliac arteries and in eight plastic aneurysmorrhaphies. In no case was evidence observed grossly of significant arterial injury from its use.

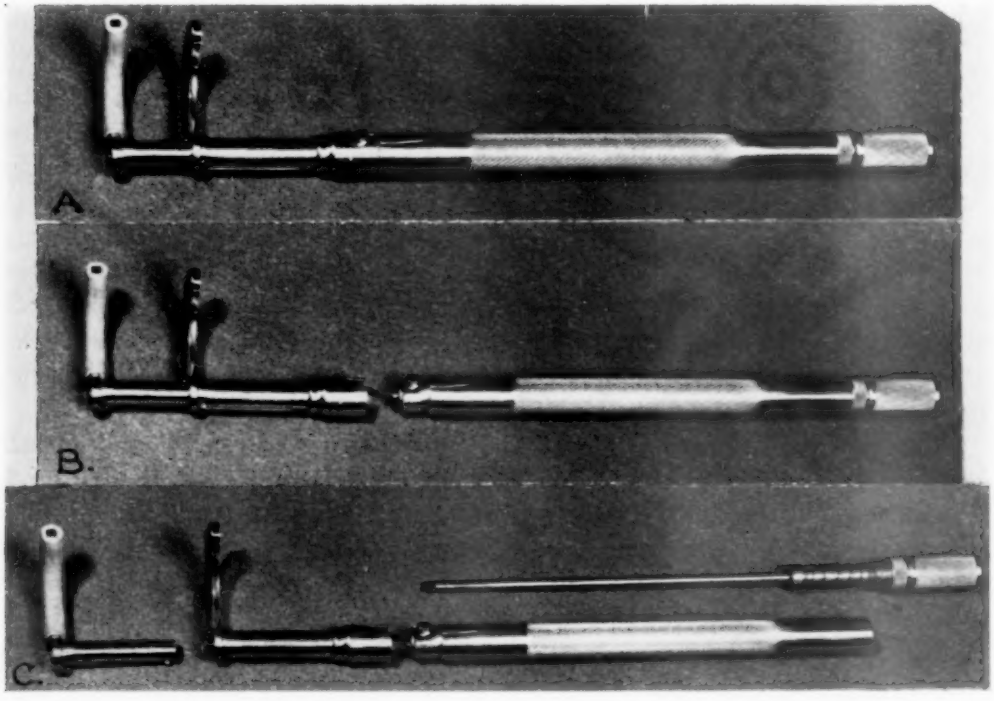


Fig. 1.—Photographs showing: *A*, clamp assembled, *B*, clamp with handle detached, and *C*, clamp disassembled for sterilization.

Experience has indicated the importance of certain operative maneuvers associated with the use of the clamp. Palpation of the aorta at the level to be occluded will often show gross arteriosclerotic changes confined chiefly to one side of the vessel. Fortunately, this is usually on the posterior wall. By placing the clamp at such an angle as to oppose the less-diseased, flexible portion of the circumference to the more-diseased, rigid portion, the tracturing effect on the vessel is minimized. When the aorta has been clamped for a prolonged period of time, intraluminal thrombosis may develop in the aorta immediately proximal to the clamp. If the clamp is partially opened by a few turns of the handle before the distal aorta is completely sutured, the rapid flow of blood will flush the clot from the proximal aorta. Clots in the aorta proximal to the clamp are not easily palpated; therefore, this maneuver is advised as a routine procedure. When the suturing of the arteries is complete, the clamp should be only partially opened again. The unavoidable bleeding from the suture line will be reduced by this method to a minimum until the few minutes required for the leakage to cease have passed. Should there be large arterial defects

evident, requiring further sutures, hemostasis may be quickly obtained by closing the blades. The clamp is not completely removed until all bleeding has been controlled.

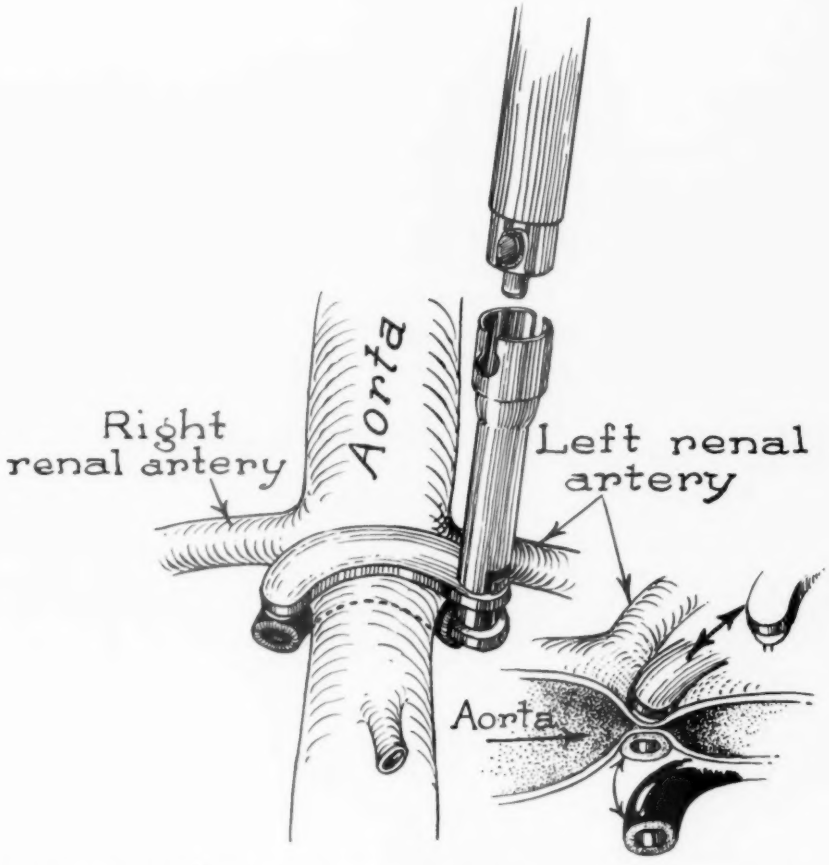


Fig. 2.—Drawing showing clamp in position below renal vessels, demonstrating advantage of convexity of blades and detachable handle.

SUMMARY

A new aorta clamp for use in operations requiring the temporary occlusion of the aorta is described.

I wish to express my appreciation to Mr. Eliot D. Green, instrument maker, University of California Medical Center, for his help in the design and construction of the clamp.

THE COMPLICATIONS OF ILEOSTOMY

ALBERT S. LYONS, M.D., AND JOHN H. GARLOCK, M.D., NEW YORK, N. Y.

(From the Surgical Service of the Mount Sinai Hospital)

INCREASING experience with the surgical therapy of nonspecific ulcerative colitis and the phenomenal rehabilitation that follows such treatment in the vast majority of patients have been factors in diminishing the antagonism on the part of both the medical profession and the lay public to the idea of a permanent ileostomy. Yet there is a considerable group of physicians who still feel that ileostomy should be carried out only as a last resort. On the other hand, the salutory results of ileostomy and colectomy have led some surgeons to the opposite extreme of advising surgical therapy for most, if not all, patients with ulcerative colitis.

We believe that both of these views are unrealistic and that the intelligent approach, based on experience with large numbers of cases, lies somewhere between these two extremes. Ileostomy to save life or to salvage those who have become chronic invalids is necessary, and spectacularly successful, but it is a procedure primarily for the treatment of advanced disease, not to be taken lightly, and should be subjected to repeated re-evaluation. Surgical therapy is indicated more for the early treatment of the complications rather than for the treatment of the early phases of the disease. As one views the satisfying results in terms of patient rehabilitation, he must not lose sight of the complications of surgical treatment in appraising the over-all picture. We have special reference to the complications of ileostomy and would like to report our experiences with this part of the problem in a series of 145 patients.

CLASSIFICATION OF COMPLICATIONS

The major complications which are specifically the result of the ileostomy itself (excluding the general postoperative complications which may follow any surgical procedure) have been divided into the "avoidable" and "inherent" groups. These studies are based on an analysis of our experiences during the past fifteen years with the surgical management of 145 patients with ileostomy.

Avoidable Complications.—

1. ***Major skin excoriations:*** In our earlier experience, marked irritations and ulcerations of the skin developed around the ileostomy stomas as a result of the constant discharge of ileal contents. The usual protective ointments and films were too frequently inadequate. Since the procedure of early

Aided by a grant from Leon Lowenstein Foundation.
Received for publication Feb. 5, 1954.

application of an ileostomy bag was adopted, the problem of early skin excoriation has practically vanished. Our incidence of 3.4 per cent refers chiefly to the first years of our experience.

We have discontinued the use of decompressing tubes sewn into the ileal stoma at the time of operation. We are now removing the occluding de Martel clamp after twenty-four to forty-eight hours and applying immediately a temporary paste-on bag. The usual rigid bag of the Rutzen or Tulin type cannot be used at this time because the ileostomy is usually too large, and because considerable amounts of drainage require too frequent changes. On occasion, use has been made of colostomy irrigating appliances which have a long tail portion to which a tube can be attached for emptying into a bedside bottle. This apparatus has sufficient depth to prevent pressure on the exteriorized segment of ileum. Recently, we have employed with gratifying success a plastic pouch with adhesive cement incorporated in one end (prepared by the Fazio Co.) which permits tailoring of the opening to any size of stoma, adheres securely to the skin, and can be discarded with each change because of small cost. These temporary bags are replaced by the permanent appliance (Rutzen, Tulin, Torbot) after several weeks or months. Thus, the surrounding skin is always protected from ileal discharge by a firmly cemented bag.

2. *Wound separations:* When, in our earlier experience, we placed the permanent ileostomy in the exploring incision, skin separations occurred often. This healing complication made application of the bag difficult, even impossible in some instances. It also became clear that any irregularity of the incision scar might interfere with the efficient adherence of any appliance. When superficial wound separations did occur, a section of rubber sheeting was cemented below or about the ileostomy, thus bridging the wound trough and permitting the cementing of a bag to the sheeting. The routine use of a stab-wound ileostomy in recent years has obviated this complication.

3. *Prolapse:* Some clinics have reported a 14.3 per cent incidence of prolapse requiring operative revision.[4] Others have found this complication to be even more frequent, 20 per cent.[7] The fact that our incidence is so incredibly low (2 per cent) suggests that the method we have been using must be responsible. The essential factor in the prevention of prolapse, as originally suggested in 1941,[1] is the adequate fixation of the raw edge of the divided mesentery of the ileum to the anterior parietal peritoneum below the site of exit of the ileostomy. When we were bringing out the ileal stoma through the original incision, this maneuver was easily accomplished, but since we began using the stab-wound technique, fixation of the mesentery to the abdominal wall has become a somewhat difficult step.

Once prolapse has occurred, correction may be extremely difficult. In one patient, four separate revisions were necessary before a desirable result was achieved. Warren and McKittrick[4] of the Massachusetts General Hospital have reported satisfactory results following reimplantation of the ileal stoma in the upper abdominal wall. The reason for success with this technique probably rests on the holding action on the ileal limb produced by making the

mesentery taut. In the few instances where we have employed this technique, it would seem that the opposite effect was produced, namely, a retraction of the ileum rather than prolapse.

When prolapse progresses too far or occurs too suddenly, there may be an increase in the diameter of the bowel, undoubtedly due to edema, with resulting constriction by the ileostomy appliance or by the abdominal scar.

4. *Fistula:* A fistula through the wall of the ileum may form below the skin level. Often an abscess in the wound surrounding the ileostomy is the first indication that a fistula has formed. The usual causes for deep fistulas are pressure of a catheter inserted in the bowel during the early postoperative period, a stitch placed at the time of operation which has inadvertently included the full thickness of the bowel, or too vigorous dilatation by the surgeon's finger. These are easily preventable causes.

Not infrequently, a fistula will occur at or above the skin level of the ileostomy stoma. Experience has shown that these are produced by the sawing action of a badly applied ileostomy bag or by one that fits too snugly. With the extended use of some of the newer and more efficient bags must come caution in their application. The rubber rim which covers the metal disk must be sufficiently wide to prevent any rubbing action against the stoma. It is important that the disk opening be at least one-sixteenth to one-eighth inch larger than needed.

In our series, the total fistula incidence was 8.9 per cent; deep fistulas occurred in 6.2 per cent of the cases, and superficial fistulas in 2.7 per cent. Operative revision was necessary in 61 per cent of these cases. Operative correction has usually not posed any difficulties. Most of our efforts have been directed toward education of the patient to prevent recurrences.

5. *Electrolyte imbalance:* Excessive functioning of the ileostomy resulting in severe acute water and mineral depletion may occur immediately following removal of the occluding clamp or later, between the first and third weeks. The principal difficulties that may ensue and may be disastrous are overfilling of the bag with digestion of the skin and severe dehydration with electrolyte imbalance. This loss may be so great and so rapid that the patient will present all the clinical signs of profound shock within one hour of onset. Death may ensue within the space of a few hours if prompt and vigorous therapy is not employed.

We have found the most effective remedy to be an intravenous injection of 500 c.c. of hypertonic sodium chloride solution (3 to 5 per cent), followed by a transfusion of whole blood. Additional electrolytes may be given after the acute emergency has been treated successfully. If excessive functioning of the ileostomy continues, adrenal cortical extracts have occasionally been of value in aiding retention in the tissues. Opium, bismuth, Banthine, or pro-Banthine aid in controlling this abnormal intestinal discharge. To prevent dislodgment of the bag by the rapid accumulation of liquid contents, it is wise to attach a large tube to the bag outlet and connect it to a bedside bottle.

The cause of this sudden or prolonged outpouring of ileal contents is not always apparent. A high ileostomy made necessary by the presence of ileitis associated with ulcerative colitis will, on a physiologic basis, show excessive watery discharge until absorptive adjustment takes place. But a low ileostomy may also show pronounced hyperactivity without obvious cause. Not infrequently, the excessive discharges, especially if very thin in consistency, precede the onset of partial obstruction. Warren and McKittrick[4] have emphasized this feature in cases with ileostomy "dysfunction."

Inherent Complications.—

1. *Obstruction:* The presence of obstruction may be heralded either by excessive watery discharge or by cessation of flow.

Minor, incomplete obstructions during the early postoperative period occur frequently. They are probably due to partial kink and the relatively rigid position of the ileostomy in the abdominal wall. The location of this type of obstruction is usually in the terminal few inches of the ileal limb and is easily relieved by introducing a thoroughly lubricated catheter into the stoma. It is sometimes necessary to tape the tube into place for a few days until bowel wall edema has subsided. It is unusual for this variety of obstruction to recur.

On the other hand, what appears to be a minor obstruction at first may in reality be the beginning of a true intestinal obstruction. The symptoms may be continuous or intermittent and are caused by a band or complete twist. If catheterization of the stoma fails to bring relief, intestinal intubation from above should be initiated immediately. The great majority of our patients responded to this form of decompression and did not require operation. There is danger, however, in waiting too long. If cramps are not relieved promptly or if the patient's general condition shows decline, operation should not be deferred.

Major obstructions requiring intestinal intubation occurred in 12 per cent of our series. One-third of these required operation, and there was a 40 per cent operative mortality. It is felt that this rate would not have been so high if we had not waited too long before operating.

2. *Retraction and superficial stenosis:* In 3.4 per cent of our patients with ileostomy, retraction and stenosis of the stoma became severe enough to require operative revision. We have been unable to determine any logical reason for this complication. In one patient who required three revisions, the ileum was permitted to project four inches beyond the skin level. Yet within six months, retraction and scarring had become so pronounced that the external opening was barely discernible on the abdominal wall. Retraction and stenosis may be accompanied by partial obstruction requiring frequent catheterization and irrigation of the distended, thickened loop of ileum proximal to the narrowed stoma. Our incidence of 13.7 per cent of combined stenosis and obstruction is lower than that reported from some clinics.[4, 7]

3. *Enteritis:* In recent years, a very disturbing complication has made its appearance, namely, enteritis near or far proximal to the ileostomy stoma.

The recurrence of ileitis in a patient who originally presented the combined form of ileocolitis would not be unexpected, but the late appearance of a localized area of small bowel disease in a patient who originally had typical nonspecific ulcerative colitis which had been treated by ileostomy and colectomy is wholly unexpected. Only 4.1 per cent of our patients developed this complication, but if its occurrence should prove to be more frequent in the ensuing years, our general concept of the surgical treatment of ulcerative colitis may very well require complete revision.

In our group, the development of enteritis became evident one to five years after completion of the therapy for the colitis. The complication must be suspected when the following symptoms appear: (1) foul discharge from the ileal stoma, (2) unexplained loss of appetite and weight, particularly if accompanied by low-grade fever, (3) excessive functioning of the ileostomy after a previously prolonged normal period, and (4) blood mixed with the fecal discharge. Increasing experience has demonstrated the effectiveness of roentgen examination after instilling barium into the stoma in establishing a diagnosis. Of course, this must be supplemented by a regular gastrointestinal radiographic examination. So far, attempts at visualization of the ileal mucosa by stomal endoscopy have not yielded much information, but we are continuing to explore this method.

Conservative therapy with the various antibiotics and corticotropic hormones has yielded questionable results. In one patient, a spontaneous remission occurred. The majority of our patients have been subjected to operation with excision of the diseased segment of bowel. Our experience to date has not been extensive enough for us to make any definitive statements about the prognosis of this complication in the conservatively treated and the surgically treated categories.

Psychologic Complications.—The attitude of the patient plays a major role in the efficient functioning of the ileostomy. It is commonly noted that an emotional upset or a temporary inability to adjust to the ileostomy will frequently be followed by a variety of ileostomy dysfunctions, which sometimes disappear dramatically after solution of the emotional problem. The patient needs help and understanding, not only in the hospital, but, particularly, after he has returned home. We have made use of two special organizations in helping us to solve some of the problems of ileostomy management.

1. *The Intestinal Rehabilitation Clinic:* There are numerous problems relating to the care of the skin, the fitting of appliances, and diet which require informed and experienced management. For this purpose, we set up a few years ago a special clinic for ileostomy and colostomy patients which meets once a week and where the ileostomy patient receives an unhurried sympathetic hearing. We have found that psychologic support is just as important as the medical and surgical therapy.

2. *The Ileostomy Club:* We have learned much about ileostomy management from the patients themselves. The Ileostomy Club, established a few years ago, has been a most progressive step. In addition to the invaluable

information obtained by both patients and doctors from the experiences of the members, the club members have found adjustment infinitely smoother, have sought and held remunerative employment, engaged in athletic activities, have married, and have borne children due to the confidence gained by association with others who have overcome the same handicap.

It is gratifying to note that others, following our lead in this interesting psychologic experiment, have formed similar clubs, notably, in Boston and Philadelphia.

CONCLUSIONS

1. Ileostomy (and colectomy) should be performed for specific indications and is not to be considered the primary form of therapy for ulcerative colitis.

2. When used to salvage invalids or to save life, ileostomy permits restoration of all normal social, sexual, and economic activities.

3. In an experience with 145 patients with ileostomy, there were forty-seven major complications, or 32 per cent. These may be classified avoidable (subject to improvement) and inherent (cause as yet unknown).

4. During a fifteen-year period, 20 per cent of all ileostomies required reoperation for complications.

REFERENCES

1. Garlock, J. H.: The Surgical Treatment of Intractable Ulcerative Colitis, Ann. Surg. **113**: 1, 1941.
2. Cattell, R. B.: The Care of Ileostomy, Lahey Clin. Bull. **4**: 45, 1944.
3. Cave, H. W.: Late Results in the Treatment of Ulcerative Colitis, Ann. Surg. **124**: 716, 1946.
4. Warren, R., and McKittrick, L. S.: Ileostomy for Ulcerative Colitis; Technique, Complications, and Management, Surg., Gynec. & Obst. **93**: 555, 1951.
5. Colcock, B. P.: Technic of Ileostomy, Surgical Practice of the Lahey Clinic, Philadelphia, 1951, W. B. Saunders Company, p. 364.
6. Lyons, A. S.: An Ileostomy Club, J. A. M. A. **150**: 812, 1952.
7. Turnbull, R. B., Jr.: Management of the Ileostomy, Am. J. Surg. **86**: 617, 1953.

A SUTURE NEEDLE WITH A DETACHABLE POINT

WILLIAM W. L. GLENN, M.D., NEW HAVEN, CONN.

(From the Department of Surgery, Yale University School of Medicine)

IN THE course of the development in the experimental laboratory of surgical techniques for the correction of intracardiac lesions, a needle with a detachable point was devised.*

The obvious advantage of a needle with a detachable point is that one may identify, and secure by feel, the point and the attached thread. Development of this needle has made it possible to insert a wire or fabric thread, with only slight displacement of the heart, from the apex to the base or from the anterior to the posterior surface, and with minimal trauma to the myocardium and its nerve and blood supply.

The essential feature of this needle is the detachable point adapted to a long, hollow steel shaft.† The shaft is moderately malleable and can be curved according to the requirements of the particular suture. These needles have been made of varying lengths, ranging from three to fifteen inches, and of varying sizes, ranging from 16 to 20 gauge. It is difficult to make the point for a needle smaller than that which will properly fit the hollow shaft of the 20 gauge steel tubing. One obvious disadvantage to such a needle is that the points are small and easily lost. It is important that the neck of the needle point fit loosely in the hollow shaft to allow the point to be detached easily from the shaft when it has passed through the tissue. The needle point is threaded with a monofilament or braided wire as shown in Fig. 1. Should one desire to pass a fiber thread with this needle, the eye of the neck of the point is threaded, but instead of passing the thread up the hollow shaft, as in the case of the wire, the neck of the needle point is forced into the hollow shaft, impinging the thread between the inner wall of the shaft and the neck. The two ends of the fiber thread, made equal in length, are allowed to hang free of the shaft. It is wise to have the thread of sufficient length so that it may be grasped in the event the point of the needle becomes detached before it has passed completely through the tissue.

During the past year this needle, as shown in Fig. 1, has been used in approximately fifty experiments concerned with the repair of intracardiac defects. Although there may be developed some further modifications of the needle as presently described, the basic design is believed to be sufficiently tested to make a report at this time.

This investigation was supported by a research grant, H-851-C3, from the National Heart Institute, of the National Institutes of Health, Public Health Service.

Received for publication, Jan. 26, 1954.

*These needles were made by Mr. Ray W. Morgan, gunsmith, 668 State St., New Haven, Connecticut.

†We are grateful to Mr. Oscar Schwidetzy of Becton, Dickinson & Company, Rutherford, New Jersey, for furnishing us with a number of long needle shafts to which the needle points were adapted.

It is possible that a needle of this type has been reported previously, although a review of suture needles[1] fails to reveal one of similar type.* A "tubular suture needle" which incorporates some of the features of the present

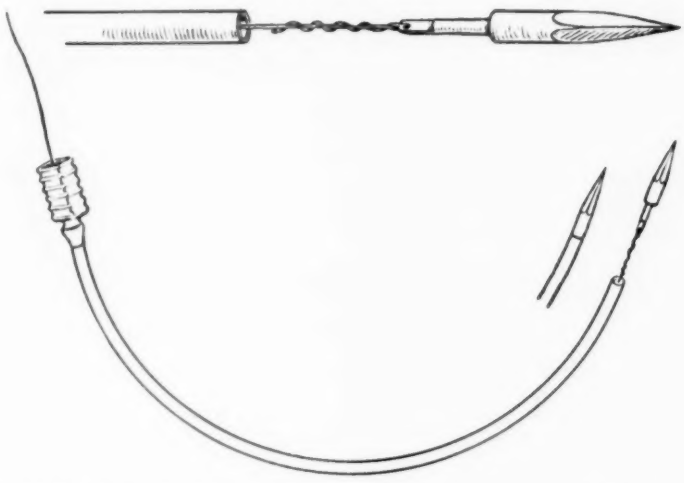


Fig. 1.—A cutting-point needle is shown, but a round point may also be used.

needle, but without a detachable point, was described by Lambert.[2] The well-known "eye-point" needle[3] also delivers the suture on the point of needle, but again, the point is not detachable.

Acknowledgment.—I am particularly grateful to Mr. Ray W. Morgan for the patience he has shown in the construction and perfection of this and other surgery instruments.

REFERENCES

1. Yoel, J.: Classification of Suture Needles, Prensa méd. argent. 33: 2228-2230, 1946.
2. Lambert, W.: Tubular Suture Needle and Holder, Lancet 2: 536, 1944.
3. Macmillan, W.: Point-eyed Suture Set, Plast. & Reconstruct. Surg. 3: 222-225, 1948.

*We apologize if we have overlooked in the literature an obvious reference to a needle similar to the one described here. Evidently such a needle is not used contemporaneously, and the purpose of this communication is to call attention to its particular value in cardiac surgical procedures. It is possible that a needle with a detachable point would have application elsewhere.

EXPERIENCE WITH A NEW, SPRAYABLE PLASTIC AS A DRESSING FOR OPERATIVE WOUNDS

STANLEY P. RIGLER, M.D., AND W. E. ADAMS, M.D., CHICAGO, ILL.

(From the Department of Surgery, University of Chicago)

SURGEONS have long sought more effective methods of dressing wounds. In 1952, Choy and Wendt[1] reported on their experience with a plastic, a modified polyvinyl chloride acetate copolymer in an ethyl acetate solvent (Aeroplast), which could be sprayed onto the wound with a spray gun or aerosol bomb. Experimental work by these authors[2] indicated that the material caused no local or systemic reactions, did not delay wound healing, provided an adequate bacteriologic border, and was easily applied by relatively untrained personnel.

The original interest in this material was directed primarily toward its utility as a burn dressing. Choy[3] has recently described its use in a number of situations, including burns, skin graft donor sites, and operative wounds. The purpose of this communication is to report our experience with Aeroplast as the sole dressing applied to a variety of operative wounds.

Procedure.—Subjects of this report were patients who underwent a variety of operations on one of the surgical services at the University of Chicago Clinics, Chicago. No attempt was made to select patients, or to compare the results obtained with the new dressing to those with conventional dressings. In each case, the original application was made while the patient was anesthetized. The plastic was sprayed onto the wound and an adjacent area of skin from an aerosol bomb, allowed to dry for thirty seconds, and a second coating applied. No gauze or tape was used in addition to the plastic.

TABLE I. TYPES OF WOUNDS

TYPE OF WOUND	NUMBER OF CASES
Thoracotomy	69
Laparotomy	27
Inguinal hernia	9
Miscellaneous	5

TABLE II. RESULTS

TYPE OF WOUND	SATISFACTORY	RE-DRESSED	ERYTHEMA	INFECTION	NECROSIS
Thoracotomy	40	15	3	6	2
Laparotomy	23	0	0	2	0
Inguinal hernia	9	0	0	0	0
Miscellaneous	5	0	0	0	0

The wounds were examined daily for evidence of healing, reaction, or infection. After seven to ten days, the dressing was peeled off, a procedure

Received for publication, Feb. 23, 1954.

involving little or no discomfort to the patient, and the sutures were removed. If the plastic showed signs of rubbing off, a new coating was applied. Reapplication, when necessary, was accompanied by local burning for a few seconds until the solvent dried.

Results.—A total of 125 separate dressings was applied from fourteen aerosol bombs, with an average yield of ten to fifteen dressings per container, depending on the length of the wound. No systemic reactions were noted. Three wounds showed a moderate degree of erythema appearing on the third to seventh postoperative day, but it is doubtful if this can be ascribed to the plastic itself. The types of wounds treated are summarized in Table I.

Fig. 1.—Transabdominal vagotomy, third postoperative day. Aeroplast dressing covering incision allows free movement of respiration and inspection of the wound.

For the most part, a single application of plastic sufficed. However, in some of the thoracotomy incisions which crossed over a bony prominence, or where the wound was subjected to rubbing and pressure because of the patient's position in bed, the dressing occasionally peeled off before the wound was

completely healed. Thus, fifteen of sixty-nine thoracotomy incisions required re-dressing. Reapplication has not been used in the last fifteen cases, and the wounds healed satisfactorily.

The over-all results are summarized in Table II. A "satisfactory" result was defined as a wound which required only one application of plastic; showed no evidence of erythema, infection, or necrosis; and healed as rapidly and with as little eschar as was to be anticipated with ordinary dressing methods. Seventy-three per cent of the wounds were deemed satisfactory, 14 per cent required a second dressing, and 13 per cent exhibited some erythema, stitch infection, or minor necrosis.

Fig. 2.—Bilateral inguinal hernia repair, fourth postoperative day. Incisions are well protected by Aeroplast dressing.

Discussion.—The objections to the classical methods of dressing wounds are well known, and need not be reiterated. Surgeons would welcome a dressing which is easily applied, subjects the patient to minimal discomfort in both its application and removal, permits observation of the wound from day to day without removing the dressing, and, at the same time, provides mechanical and

bacteriologic protection equal to that of the ordinary dressing. Our experience with Aeroplast indicates that this material is satisfactory in all these respects. The incidence of erythema and superficial infections which we observed is no greater than in our experience with other types of dressings, and is not attributable to the plastic itself.

Fig. 3.—Thoracotomy, for pulmonary inflammatory disease, fourth postoperative day. Adhesive tape surrounds drains. Aeroplast dressing covers and protects the incision. This allows free access to the chest for daily examinations and produces no restriction of respiratory movements.

In thoracic surgery, two additional factors become important. It is desirable to be able to percuss and auscultate the chest of the postthoracotomy patient. Ordinary dressings, abundant in gauze and adhesive tape, provide a real obstacle. But plastic, sprayed over the wound and a small area of adjacent skin, permits ready examination of the entire chest. Further, the plastic dressing results in no limitation of motion of the chest, and allows for adequate ventilation postoperatively.

The matter of convenience and cost is of some importance. Aeroplast containers are easily stored, require less space than conventional dressing mate-

B.

A.

Fig. 4.—*A* and *B*. Two views of thoracotomy wound for repair of coarctation of aorta thirteen days following operation. Note complete healing of the wound by primary intention.

rials, and need not be sterilized. We have computed the approximate cost of dressings in our hospital, and have found that a thoracotomy dressing of the usual type costs approximately fifty cents, while an Aeroplast dressing costs roughly forty-five cents.

Recently, Heifetz and associates[4] have pointed out that many surgical wounds heal adequately without any dressing. As a result of their experience, they cited a number of rigid indications for the "no dressing" technique, including strict atraumatic surgery, absence of oozing from the wounds, lack of drains, and so forth. For the many wounds which do not meet these requirements, it is our feeling that plastic has real advantages over conventional dressings.

CONCLUSIONS

Experience with a sprayable plastic dressing applied to a variety of operative wounds indicates that this dressing is easily and rapidly applied. It permits adequate wound healing, with no greater incidence of superficial wound infections than that observed with the customary type of dressing. In addition, this method permits day-to-day observation of the wound without removal of the dressing, and allows the thoracic surgeon to examine the postoperative patient without the encumberance of tape and gauze. The cost of the plastic dressing is somewhat less than that of the commonly used type. Conservation of space for dressing material is also an advantage worth consideration.

SUMMARY

This report deals with experience in use of a plastic dressing in 110 separate operative wounds of various types. A single application sufficed in all but fifteen cases.

No instances of systemic or clear-cut local reactions were observed.

Satisfactory results, with no evidence of erythema, infection, or necrosis, were obtained in the majority of cases.

Advantages of this type of dressing are briefly discussed.

We wish to acknowledge grateful appreciation for the assistance of Dr. Peter V. Moulder, Dr. Clair Basinger, and Dr. John Ziegler in this study.

The material used in this study was furnished by the Aeroplast Corporation, Dayton, Ohio.

REFERENCES

1. Choy, D. S. J., and Wendt, W. E.: A New Local Treatment of Burns, U. S. Armed Forces M. J. **3:** 1241 (Sept.) 1952.
2. Choy, D. S. J.: Rates of Wound Healing When Standard and Experimental Burn Dressings Were Used, U. S. Armed Forces M. J. **4:** 599 (April) 1953.
3. Choy, D. S. J.: Clinical Trials of a New Plastic Dressing for Burns and Surgical Wounds, Arch. Surg. **68:** 33, 1954.
4. Heifetz, C. J., Richards, F. O., and Lawrence, M. S.: Wound Healing Without Dressings, Arch. Surg. **67:** 661, 1953.

Case Reports

THE USE OF CORTISONE IN THE TREATMENT OF SARCOIDOSIS OF THE SPLEEN PRIOR TO SPLENECTOMY

SAUL KAY, M.D., AND HENRY P. ROYSTER, M.D., RICHMOND, VA.

(From the Laboratory of Surgical Pathology and the Department of Surgery, Medical College of Virginia)

THE beneficial effects of cortisone and ACTH for diseases marked by allergic manifestations are well established. It is only logical, therefore, that Boeck's sarcoid should have been given clinical trial with these drugs, since many clinicians believe that sarcoidosis is due to an allergic response to some foreign substance (protein or otherwise) introduced into the body.

During the past two years, a number of publications have appeared extolling the use of cortisone and ACTH in sarcoidosis.[1, 2, 5-12] These papers are principally American, although a few are in the British,[2] Scandinavian, German, and French literature.[1] Apparently, the response to the drugs is most favorable with pulmonary and eye lesions, although decrease in size of peripheral lymph nodes and spleen was also noted,[8, 9] as well as regression in cutaneous manifestations.[1, 11] In none of Michael's[7] ten patients, or the fifteen reported by Shulman and associates,[9] was there subsequent development of tuberculosis. Michael nevertheless cautioned against the indiscriminate use of cortisone except in those cases with symptoms particularly associated with pulmonary and eye lesions. This author also noted that there was a marked tendency to relapse on cessation of therapy.

Almost all investigators agreed that cortisone therapy hastens healing of the sarcoid lesions, as evidenced histologically by smaller and fewer tubercles, associated with more fibrosis and hyalinization. Sometimes hyaline change of the stroma with absence of tubercles is the only finding. A case presented by Koszalka and Fortney[5] showed no alteration of an ultimate fatal course, but no active lesions were found at autopsy. The authors concluded that the scarring and collagen found in the tissues indicated spontaneous healing rather than an effect due to drug therapy.

In a detailed and most complete study of fifteen patients with generalized sarcoidosis by Shulman and co-workers,[9] the spleen was palpable in nine. The size of the organs ranged from 1 to 6 cm. below the left costal margin. ACTH was the principal drug utilized, and decrease in size of the spleen was noted as early as the second day. In seven cases the spleen became impalpable and, despite the partial return of the enlargement in three, none could be felt at the most recent follow-up. The authors stressed that intensive treatment should be given at the start in order to insure maximal improvement.

Received for publication Jan. 20, 1954.

Stiltzbach's[10] paper concerned thirteen patients with sarcoidosis of the generalized type. Two of these had splenomegaly, and cortisone failed to reduce the size of the spleen, although the drug was used for sixty-three days in dosage of 100 to 150 mg. daily. All patients nevertheless seemed to improve subjectively and objectively, with better response in fresh lesions. There were pre- and posttreatment biopsy specimens available in eight patients, and the author concluded that the most favorable effect appeared to occur in peripheral lymph nodes.

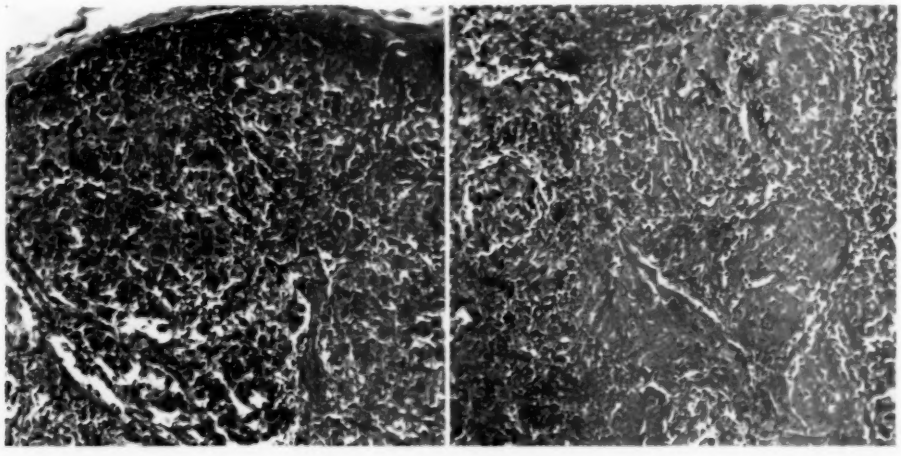
There are several reports in the literature dealing with sarcoidosis of the spleen in which the pathologic findings are almost exclusively in the spleen, and the patient complains principally of splenomegaly.[3, 4] The spleen can attain huge dimensions, and the largest spleen reported with this disease weighed 4,800 grams.[4] The case about to be reported furnished us an opportunity to study the effect of cortisone on a severe splenomegaly due to Boeck's sarcoid. Since there is a definite operative hazard in surgical removal of a markedly enlarged spleen, it was hoped to reduce this hazard by attempting to shrink the size of the spleen with preliminary cortisone therapy. Despite the fact that dissemination of the disease was minimal from the clinical standpoint, the report of Shulman and associates[9] encouraged us to attempt a course of cortisone prior to surgery.

CASE REPORT

First Admission.—C. T., a 26-year-old Negro woman, was admitted to St. Philip Hospital on Aug. 26, 1953, with complaints of fullness in the abdomen for the previous six months. About six weeks prior to admission she noted postprandial abdominal discomfort associated with gas pains. Because of increasing abdominal size, the patient thought she was pregnant. Physical examination revealed a massively enlarged and firm spleen extending well down into the pelvis, and palpable on pelvic examination. The liver was enlarged to two fingerbreadths below the costal margin. The axillary, inguinal, and left epitrochlear nodes were enlarged. Laboratory findings included hemoglobin values from 11 to 12.9 Gm., total white cell count from 3,600 to 6,000, and red blood cell count of 4,710,000. The differential white count was essentially normal. Bone marrow smears revealed marked eosinophilia. The highest eosinophil count was 649 per cubic millimeter. The sedimentation rate was 54 mm. per hour. The serum albulin-globulin ratio was 3.2:4.5 Gm. The platelet count was 340,000, with normal bleeding and clotting time. Liver function studies showed 4 plus cephalin flocculation, thymol turbidity of 9 units, 9 per cent retention of Bromsulphalein dye at the end of forty-five minutes, elevated alkaline phosphatase (11.2 units), and a decrease in free cholesterol. The serum bilirubin was normal, and the prothrombin time was 50 per cent of normal. The left epitrochlear node was excised on the third hospital day, and a diagnosis of Boeck's sarcoid was established. An aspiration biopsy of the spleen was unsatisfactory. One week later it was decided to perform an exploratory laparotomy for the purpose of obtaining biopsies of both the liver and spleen. Pathologic examination revealed the presence of sarcoidosis in both these organs. Since it was thought that surgical removal of the spleen at its present size might be hazardous, the patient was discharged Sept. 12, 1953, with at attempt to reduce the size of the spleen by means of cortisone therapy. Twenty-five milligrams of oral cortisone was prescribed three times daily, and the patient was followed in the medicine clinic. This medication was supplemented by KCl, 0.6 Gm. three times daily, and a salt-free diet.

Second Admission.—The patient was readmitted Oct. 19, 1953, for splenectomy after she had been on cortisone therapy for about five weeks. The spleen was still markedly enlarged, but appeared to be smaller by two to three fingerbreadths, according to one observer.

The liver had not changed in size. There were no complaints, and the patient was alert, cheerful, and cooperative. Laboratory findings prior to operation included a normal bleeding and clotting time, and prothrombin concentration 75 per cent of normal. The hemoglobin was 11.8 Gm., with total white count of 5,600 and normal differential. The platelet count was 360,000 and the reticulocyte count 3 per cent. The albumin-globulin ratio was 3.4:5.1. Chest roentgenogram was normal with no suggestion of Boeck's sarcoid. The patient was operated upon on the third hospital day, when a splenectomy and wedge-shaped biopsy of the liver were performed. During the procedure, the surgeon (H. P. R.), who had performed the previous laparotomy, was able to compare the size of the spleen prior to and after cortisone. There was a definite reduction in size of the spleen to approximately one-half its previous size. Following operation, the white cell count rose to 22,700. The highest platelet count was 473,000, and the highest eosinophil count was 193 per cubic millimeter. Two days prior to discharge the white count was still elevated, with a differential of 92 polymorphonuclear leukocytes, 7 lymphocytes, and 1 eosinophil. Cortisone was continued during this hospital stay with gradual reduction of dose until Oct. 29, 1953, when the last dose was given. The patient was discharged Oct. 31, 1953, to be followed in the medicine clinic.



A. *B.*

Fig. 1.—*A*, Epitrochlear lymph node prior to cortisone therapy. Sarcoid tubercles are visible beneath the capsule. (×120; reduced ⅙.)

B, Pancreaticolienal lymph node after cortisone therapy. While tubercles are clearly outlined, they are largely hyalinized and partly confluent. (×120; reduced ⅙.)

PATHOLOGIC FINDINGS

Tissue From the First Admission.—

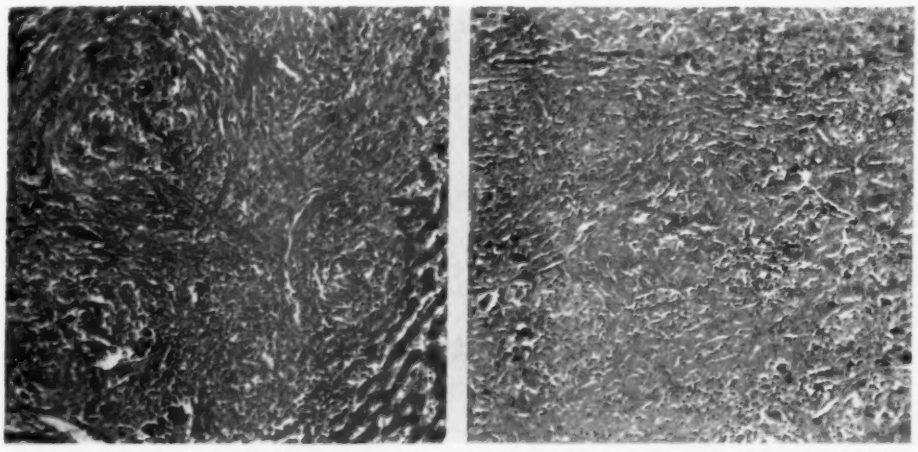
Gross: (Aug. 29, 1953) The specimen consisted of a lymph node removed from the epitrochlear region and measuring 1.10 by 0.5 by 0.5 cm. Cut section showed a smooth, shiny capsule and yellowish tan lymphoid parenchyma.

Microscopic: Section showed considerable replacement of the lymph-node architecture by sarcoid tubercles without caseation. Some areas revealed partial to complete hyalinization of the tubercles, as well as tongues of hyaline material sinuating between tubercles (Fig. 1, *A*).

Gross: (Oct. 4, 1953) The specimen consisted of a wedge-shaped biopsy of both the liver and spleen. The liver biopsy measured 1.5 by 1.5 by 0.6 cm. The capsule was smooth but showed tiny white plaques on the surface. Cut section showed glistening brown parenchyma. The spleen had been previously sectioned so that it was now in four pieces, the largest being 1.7 by 1.7 by 1.2 cm. The serosal surface was blue and shiny, and the splenic pulp was firm and dry.

Microscopic: The liver showed disruption of the usual architecture by the presence of tubercles similar to those seen in the lymph node (Fig. 2, *A*). There was considerable

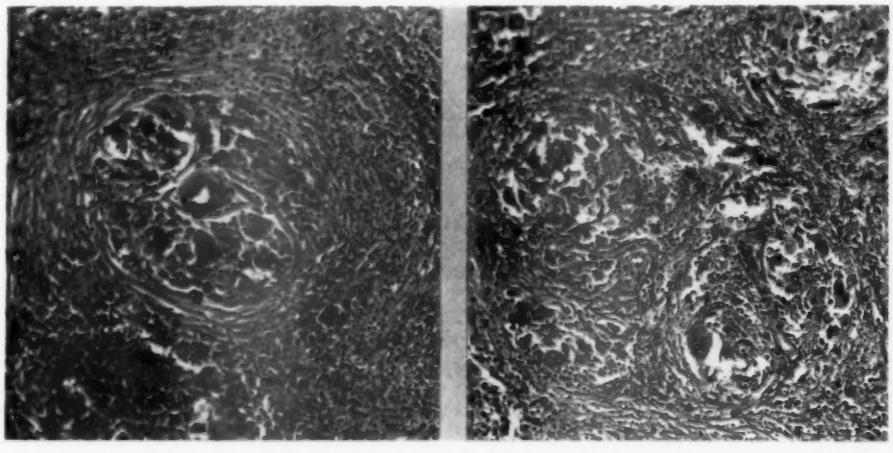
hyaline scarring of some tubercles, and fibrous tissue separated one tubercle from another. Caseation necrosis was not seen. A few multinucleated giant cells were noted both within tubercles and within fibrous scarred areas. The tubercles appeared to have their origin in portal areas with extension into neighboring liver parenchyma. The splenic parenchyma was similarly replaced by discrete and confluent tubercles composed of epitheloid cells, which were often conglomerated to form multinucleated giant cells (Fig. 3, *A*). Asteroid inclusions were not identified. Considerable fibrosis associated with recent hemorrhage was seen between tubercles.



A. *B.*

Fig. 2.—*A*, Liver prior to cortisone therapy. Tubercles are clearly visible above cords of liver cells in lower right margin of photomicrograph. (×120; reduced 1/6.)

B, Liver after cortisone therapy. Tubercles are largely represented by hyaline scars. (×120; reduced 1/6.)



A. *B.*

Fig. 3.—*A*, Spleen prior to cortisone therapy. (×120; reduced 1/6.)

B, Spleen after cortisone therapy showing no appreciable microscopic differences. (×120; reduced 1/6.)

Tissue from Second Admission.—

Gross: (S-53-7421) The specimen consisted of an entire spleen, and liver biopsy. The spleen weighed 1,090 grams and measured 27.5 by 12 by 5 cm. It had a nodular, shiny, glistening, capsular surface. Cut section revealed a meaty, red-brown tissue having an exaggerated lobular pattern. Five hilar lymph nodes were identified, the largest 2.5 by

1 by 0.8 cm. The liver biopsy was a small, wedge-shaped piece of tan tissue with a somewhat irregular surface and measuring 1.7 by 1 by 0.5 cm. Cut section showed slight increase in fibrous tissue.

Microscopic: A comparison of present sections with the previous biopsies of the liver, spleen, and lymph nodes showed appreciable differences only in the lymph nodes and liver (Figs. 1, *B* and 2, *B*). In these tissues there were fewer tuberculoid lesions, and these were much less discretely outlined. Hyaline scarring was more marked, and there was evidence that the pathologic process was healing, since in some areas no tubercles could be made out. (Compare Fig. 2, *A* and *B*.) The spleen was practically unchanged (Fig. 3, *B*) except for occasional evidence of perivascular "rings" of broad hyaline bands (Fig. 4).

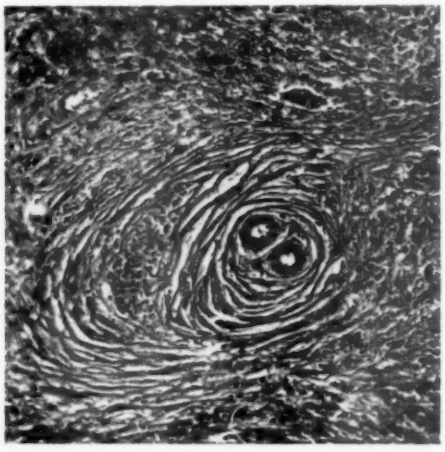


Fig. 4.—Spleen after cortisone therapy. One field reveals perivascular hyaline "rings," and possibly represents features of healing of the sarcoid process. (×120; reduced ⅙.)

DISCUSSION

In the past it has generally proved worth while to treat patients with sarcoidosis of the spleen by splenectomy whether or not the diagnosis was made preoperatively. Where the disease is principally confined to the spleen, the complaints of the patient are largely due to the enlarged organ and associated symptoms of hypersplenism. As a rule, most patients will do fairly well after splenectomy, and one of us (S.K.) has had an opportunity to study the follow-up of a patient during a twenty-three year period after splenectomy. This patient, while exhibiting a number of minor complaints during this extended period, has had no serious impairment of health due to sarcoidosis. It is also true, however, that a few patients may have progression of the disease at a slow, unrelentless pace despite splenectomy.

To the best of our knowledge, this is the first case reported in which a course of cortisone therapy was attempted prior to contemplated surgery. Based on previous reports in the literature, we believe that the dosage used in this case might have advantageously been higher and of longer duration in preparation for surgery. It would certainly have been desirable to reduce the size of the spleen to a clinically impalpable size, and theoretically this should have been possible. The failure to reduce the size of the spleen in Siltzbach's[10] two cases of splenomegaly is unexplained.

Further indication that the dosage employed may have been inadequate could be gleaned from a study of the microscopic sections of lymph nodes, liver, and spleen. Comparisons of sections prior to and after cortisone showed definite evidence of healing of the sarcoid process only in the liver and lymph nodes. Essentially, the process in the spleen remained unchanged, although an increase in fibrous stroma must have taken place, since only by such scarring can an appreciable reduction in size be accounted for.

SUMMARY

A case of sarcoidosis of the spleen is presented in which cortisone therapy was administered for the purpose of reducing the size of the spleen prior to surgery. Tissues of lymph nodes, liver, and spleen were available for comparison before and after a five-week course of the drug.

ADDENDUM

At the patient's last admission to the Clinic, April 22, 1954, she was found to have a liver enlarged seven fingerbreadths below the costal margin. Her axillary nodes have also enlarged, and she has developed a chronic cough. Fluoroscopy of the chest revealed hilar findings compatible with parenchymal sarcoid disease. The patient is being admitted to the hospital for study, and another course of cortisone therapy is contemplated.

REFERENCES

1. Benard, H., Rambert, P., and Habib, G.: Action de l'ACTH sur les lésions cutanées et ganglionnaires dans uncas de maladie de Besnier-Boeck-Schaumann, Bull. et mém. Soc. méd. d. hôp. de Paris **68**: 49-52, 1952.
2. Dolphin, A., and Heathfield, K. W. G.: Sarcoidosis Treated With Cortisone; Report of a Case, Lancet **2**: 1160-1162, 1952.
3. Friedman, M.: Sarcoidosis of the Spleen. Report of a Case With Autopsy and a Study of Intracellular "Asteroid Bodies," Am. J. Path. **20**: 621-635, 1944.
4. Kay, S.: Sarcoidosis of the Spleen. Report of Four Cases With a Twenty-three Year Follow-Up in One Case, Am. J. Path. **26**: 427-443, 1950.
5. Koszalka, M. F., and Fortney, A. C.: Sarcoidosis: Treatment With Cortisone, ACTH and Urethane, Dis. of Chest. **23**: 444-451, 1953.
6. Lovelock, F. J., and Stone, D. J.: Cortisone Therapy of Boeck's Sarcoid, J. A. M. A. **147**: 930-932, 1951.
7. Michael, M.: The Treatment of Sarcoidosis With Cortisone, Tr. Nat. Tuberc. A. **47**: 65-68, 1951.
8. Miller, M. A., and Bass, H. E.: Effect of Acthar-C (ACTH) in Sarcoidosis, Ann. Int. Med. **37**: 776-784, 1952.
9. Shulman, L. E., Schoenrich, E. H., and Harvey, A. M.: The Effects of Adrenocorticotropic Hormone (ACTH) and Cortisone on Sarcoidosis, Bull. Johns Hopkins Hosp. **91**: 371-415, 1952.
10. Siltzbach, L. E.: Effects of Cortisone in Sarcoidosis. A Study of Thirteen Patients, Am. J. Med. **12**: 139-160, 1952.
11. Small, M. J.: Favorable Response of Sarcoidosis to Cortisone Treatment, J. A. M. A. **147**: 932-937, 1951.
12. Sones, M., Israel, H. L., Dratman, M. B., and Frank, J. H.: Effect of Cortisone in Sarcoidosis, New England J. Med. **244**: 209-213, 1951.

PLASMA CELL MYELOMA OF VERTEBRAE WITH AMYLOID TUMOR, PRODUCING PARAPLEGIA

Report of a Case

Victor Pino, M.D., Columbus, Ohio

(From the Department of Surgical Pathology, College of Medicine, Ohio State University)

A CASE of plasma cell myeloma of the spine with amyloid tumor has recently been encountered at the University Hospital. Because of the infrequent occurrence of this condition, the case is here presented.

CASE REPORT

History.—H. T., a 49-year-old white man, was admitted to the neurosurgical service of the University Hospital on April 4, 1953, complaining of paralysis of the lower extremities. He had first noticed numbness of the plantar aspect of the feet in October, 1952. This was followed by progressive weakness and numbness of the lower extremities, and five weeks prior to admission, the patient was unable to walk. There had been occasional incontinence of urine and feces.

He gave no history of injury, weight loss, or any seriously incapacitating disease prior to the onset of the present illness. Until the onset of weakness in the legs, the patient had been operating an air hammer for several years.

Physical Examination.—The patient did not appear acutely ill; temperature, pulse, and respiration were within normal limits. The blood pressure was 110/65, weight 148 pounds, height five feet, eleven inches. There was a small raised nodule at the level of the right transverse process of the tenth dorsal vertebra, said to be present for several years. Pressure caused partial blanching. Subsequent histologic examination revealed this to be a basal cell carcinoma.

Neurological examination disclosed paralysis of both lower extremities, except for slight extension and adduction of the right thigh and extension of the right great toe. Mild spasticity, which increased with any attempted movement, and sustained patellar and ankle clonus were present bilaterally. Slight muscular atrophy was present in both calves. Knee and ankle reflexes were markedly hyperactive. The Babinski reflex was positive bilaterally; abdominal and cremasteric reflexes were absent. Pain, temperature, and light touch sensations were impaired below the level of the tenth thoracic vertebra, except for an intact area extending from the fifth lumbar vertebra to the lower sacral region. Proprioception as well as vibratory senses was absent in both legs. The soles of the feet were markedly hyperesthetic to sharp and dull stimuli.

Laboratory Studies.—Serologic reactions of the blood for syphilis were negative. The urine was normal. No search for Bence Jones protein was made on admission. The hemogram showed 9,600 leukocytes per cubic millimeter with a normal differential count and 6.21 million erythrocytes per cubic millimeter. The hemoglobin measured 16.9 Gm. per 100 c.c. Blood chemistries, including serum calcium, phosphorus, alkaline and acid phosphatase, albumin, and globulin, were all within normal range. Spinal fluid withdrawn by lumbar puncture on the day of admission was under normal pressure, and it was clear and contained 19 erythrocytes and 1 leukocyte per cubic millimeter. Protein level was 60 mg. per cent.

Roentgen Examinations.—Anteroposterior radiograph of the chest revealed a well-circumscribed area of soft tissue density, measuring 4 cm. in greatest diameter, located immediately to the left of the ninth and tenth vertebral bodies. A destructive process involving the posterior portion of the ninth and tenth left ribs was also noted. An attempt

Received for publication July 31, 1953.

at myelography via the lumbar route was unsuccessful; the contrast media was injected extradurally. Thereafter a cisternal myelogram was made and a complete block demonstrated at the level of the eighth dorsal body with extramedullary compression on the left. The lesion was identified as an extramedullary tumor, having dumbbell characteristics, most likely a neurofibroma.

Operation.—A laminectomy (eighth through tenth thoracic vertebrae) was performed on April 16, 1953. A well-vascularized tumor, involving the soft tissue, muscles, and bone, was found at the site of the incision. This growth encircling and compressing the spinal cord extended from the eighth to the tenth thoracic vertebrae, and was removed piecemeal.

Fig. 1.—Photomicrograph of the tumor showing collections of plasma cell and masses of amyloid, often bordered by multinucleated foreign-body giant cells. (×64; reduced ⅙. Hematoxylin and eosin stain.)

Pathologic Description.—Grossly the specimen consisted of several pieces of pink-gray tissue; the largest measured 3 by 2 by 2 cm. It was firm in consistency and cut with gritty sensation. Also included were several fragments of bone. Histologic sections of the tissue were composed largely of rounded masses of pink-staining hyaline material, often bordered by multinucleated foreign-body giant cells (Fig. 1). Scattered throughout the hyaline material there were collections of plasma cells having an abundant metachromatic cytoplasm and eccentric nuclei (Fig. 2). The chromatin was disposed in clumps about the periphery, giving the characteristic "cartwheel" appearance to the nuclei.

In sections stained with methyl violet, the hyaline material gave the red-purple color characteristic of amyloid. Numerous deposits of amyloid were also seen in the decalcified bone.

Histopathologic diagnosis was plasma cell myeloma with amyloid tumor.

Subsequent Course.—Following the operation, the patient received x-ray therapy over the site of the lesion. He will receive a total of 4,000 r, in doses of 200 r, twice a week. A complete radiographic survey has failed to disclose any further lesion in the bones, and repeated urine examinations for the presence of Bence Jones protein have been negative. Bone marrow biopsy and smears showed no abnormalities. Blood chemical studies have remained within normal limits.

The patient made an uneventful recovery. His general condition improved. He gradually regained sensation and muscular power in the legs and on discharge was able to walk with the aid of canes.

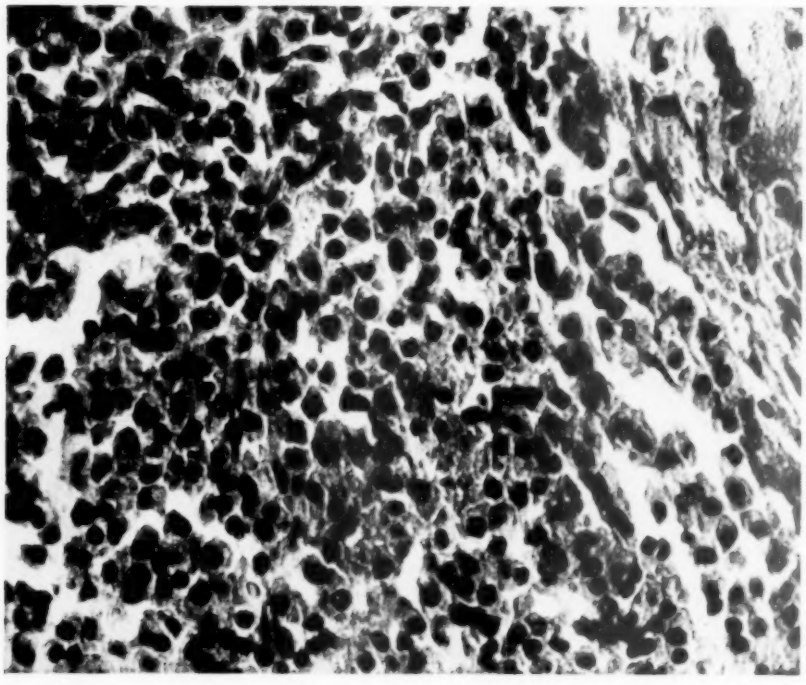


Fig. 2.—Photomicrograph at higher magnification showing a collection of plasma cells. (×430; reduced ⅕. Hematoxylin and eosin stain.)

COMMENT

Nontraumatic lesions of the spine that result in paraplegia are numerous and are usually classified as intramedullary and extramedullary. The most common intramedullary lesions are gliomas of various types. Among the extramedullary lesions, those involving the vertebrae are tuberculosis of the spine, primary and secondary tumors, and herniation of nucleus pulposus. Many cases of plasma cell myeloma of the vertebrae have been reported in the literature.[1-3] However, association of this condition with amyloid tumor is an uncommon finding. In a review of sixty-six cases of surgically treated myeloma, Dahlin and Doekerty[4] found fourteen associated with amyloid tumor; of these, only three involved the vertebrae, and no mention is made of any neurological findings.

SUMMARY

A case of plasma cell myeloma of the spine with amyloid tumor-producing paraplegia is presented. The condition of the patient improved considerably after decompression of the cord by surgical removal of the tumor.

REFERENCES

1. Christopherson, W. M., and Miller, A. J.: Re-evaluation of Solitary Plasma Cell Myeloma of Bone, Cancer 3: 240-252, 1950.
2. Raven, R. W., and Willis, R. A.: Solitary Plasmocytoma of the Spine, J. Bone & Joint Surg. 31-B: 369-375, 1949.
3. Willis, R. A.: Solitary Plasmocytoma of Bone, J. Path. & Bact. 53: 77-85, 1945.
4. Dahlin, D. C., and Dockerty, M. B.: Amyloid and Myeloma, Am. J. Path. 4: 581-594, 1950.

ARTERIAL RECONSTRUCTION (THROMBOENDARTERECTOMY) IN ARTERIOSCLEROTIC VASCULAR DISEASE

A Report of Two Successful Cases

A. D. McKenzie, M.D., and H. Rocke Robertson, M.D.,
Vancouver, British Columbia

(From the Department of Surgery, Faculty of Medicine, University of British Columbia, and the Department of Surgery, Vancouver General Hospital)

With the prolongation of life expectancy effected by medical advances has come an increase in the medical problems of old age. Many of these are manifestations of arteriosclerosis.

Arteriosclerotic disease in the lower extremities may occasion chronic arterial insufficiency with claudication, coldness, and trophic changes, or a more acute insufficiency which threatens the limb. Ischemic arteriosclerotic limbs have been treated with rest, meticulous foot care, anticoagulants, and attacks on the nervous system, chemical or surgical. When these measures have failed, and this is not infrequent, an above-knee amputation is our only recourse.

In the last five years, numerous reports in the French literature by dos Santos,[2] Leriche,[5] Bazy,[1] and others have appeared reporting direct attack on the arteriosclerotic vessels. In the last year, there have been a few reports in the American literature, particularly by Wylie[6, 7] of California, of the use of similar procedures. Successful restoration of adequate blood supply was accomplished in several cases and maintained up to thirteen months.

The direct approach to arteriosclerosis is not applicable in all cases. Obviously, in diffuse arteriosclerosis with generalized reduction in the blood flow, surgery is of no avail. However, when the disease has progressed unevenly, or local thrombosis has occurred, resulting in a segmental occlusion, then surgery may be useful. Trauma may be a factor in the causation of segmental occlusion. History and physical examination may differentiate the diffuse and the local types, but most cases will require aortography or arteriography for accurate selection. Visualization of the arterial tree also reveals whether there is an adequate lumen proximal and distal to the site of occlusion. Little is to be gained by reconstituting a vessel where there is peripheral thrombosis or extensive arteriosclerotic occlusion. Vessels which have been surgically treated for segmental occlusion include the aortic bifurcation (Leriche's syndrome), the iliac vessels, and the superficial femoral and popliteal vessels.

Restoration of blood flow in occluded arteriosclerotic vessels has been achieved either by resection of the occluded segment and introduction of a graft or by thromboendarterectomy. The former has obvious technical difficulties, namely, securing sound anastomoses with a sclerotic vessel. Thromboendarterectomy is removal of the intimal arteriosclerotic layer with any luminal thrombus, leaving the media and adventitia to be reconstituted as the

Received for publication, Feb. 1, 1954.

vessel wall. The formation of plaques in the intimal layer, the media being only secondarily affected, makes this feasible. A cleavage plane between the diseased inner layer and the media is frequently apparent on incising the vessel, or it can be developed with ease. On stripping the diseased lining, a surprisingly smooth surface remains. Wylie[7] has shown that a film of coagulated blood early covers this surface, to be replaced in four or five days by an intima-like membrane. Restoration of the arterial wall is by simple silk suture. Various techniques of performing this stripping have been described, including proximal and distal transverse incisions with reaming (dos Santos[2]), multiple incisions with rolling back the outer layer from the diseased intima like a shirt sleeve (Julian[4]), and a longitudinal incision extending proximal and distal to the diseased segment (Reboul[5]). Arterial reconstruction and immediate limb salvage have been repeatedly proved possible. Reported longer-term results are rare.

A. *B.* *C.*

Fig. 1.—Case. 1. *A*, Preoperative arteriogram, June, 1952. *B*, One month postoperative arteriogram, July, 1952. (Recheck at eighteen months, December, 1953, shows lumen maintained.) *C*, Eighteen months postoperative arteriogram, December, 1953.

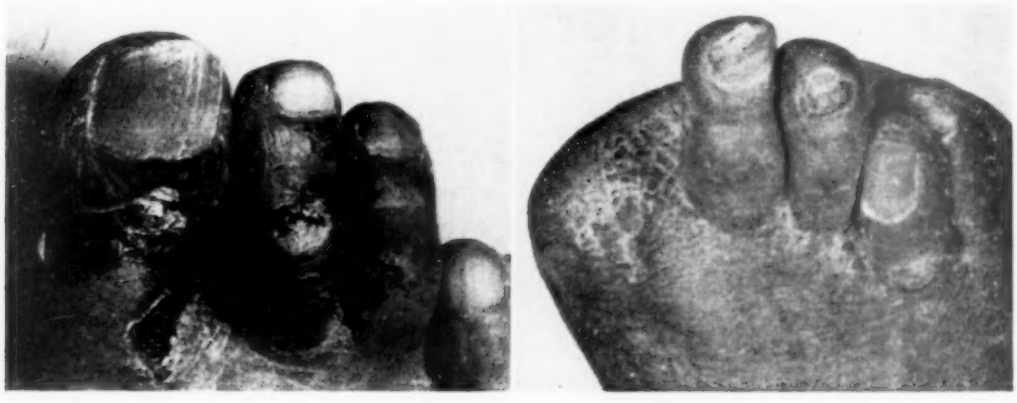
We wish to report one unsuccessful and two successful cases of femoral thromboendarterectomy with sustained good results. We have used the longitudinal incision as the simplest, and effected the closure with a continuous suture of No. 00000 Deknatel silk on an atraumatic needle. Heparin is used locally during the operation and postoperatively for about four days.

CASE 1.—K. T. (No. 80689), a 69-year-old man, was admitted May 16, 1952, to the Vancouver General Hospital complaining of pain and coldness in the right leg for five days. This leg had previously troubled him with cramps in the calf for a two-month period. Examination revealed normal heart and blood pressure, good pulses in the left leg, but absent pulses below the femoral artery in the right leg. There were well-marked changes of ischemia in the affected leg, which was cold, blue, blanched on elevation, and anesthetic over the dorsum of the right foot, and which revealed marked muscular atrophy of the right calf.

On admission the condition was diagnosed as arteriosclerosis plus thrombosis of the distal femoral artery, and the patient was treated by repeated lumbar blocks. These were relatively ineffectual, and a right lumbar sympathectomy performed five days later resulted in some slight improvement in color and skin temperature. At his insistence the patient was allowed home for one week following this operation, but had to be readmitted with acute ischemic changes in the right big toe and a cellulitis over the dorsum of the right foot.

On readmission, an arteriogram (Fig. 1, *A*) was made showing an occlusion of the distal femoral and proximal popliteal artery. Clinically, the leg was in a critical state of arterial insufficiency with frank gangrene of the first toe and ungual regions of the third and fifth toes (Fig. 2, *A*). An above-knee amputation was recommended to the patient, but obdurately refused.

On June 16, 1952, the femoropopliteal artery was exposed with division of the right adductor magnus muscle insertion. The artery was found pulsatile in Hunter's canal, but indurated for approximately 10 cm. from the hiatus in the adductor to the lower reaches of the popliteal vessel. At the lower end it again became pliable, but nonpulsatile. Proximal and distal control of the vessel was gained, and a longitudinal incision slightly longer than the indurated area was made into the lumen of the artery. Recent, firm, black thrombus occupied the narrow lumen. This was removed, and the diseased inner layer of the vessel was teased and stripped out. The vessel was closed with a simple continuous 00000 suture of silk, over which Gelfoam was laid and held in position with an occasional interrupted stitch in the sheath of the vessel.



A. *B.*

Fig. 2.—Case 1. *A*, Preoperative condition of forefoot, June, 1952. *B*, Postoperative condition of forefoot, December, 1953.

The patient was maintained on heparin and Dicumarol for three weeks postoperatively. A postoperative wound hematoma required evacuation and secondary wound suture. Amputation of the right great toe was performed six weeks postoperatively, as the gangrene previously present had involved the distal interphalangeal joint. It was noted that the vascularity of tissues at this operation was normal, and healing was uneventful. An arteriogram in July, 1952, one month after operation, showed clearing of the lumen with a good passage through the principal vessels of the leg (Fig. 1, *B*).

During the eighteen months since operation, the patient has shown progressive improvement. Early edema and ischemic foot pain have subsided, and he enjoys good function. On the last examination, December, 1953, the foot was healthy. The popliteal pulse was palpable, and continued patency of the femoropopliteal axis was confirmed by arteriography (Fig. 1, *C*).

CASE 2.—F. J. (No. 42512), a 67-year-old man, had a fracture of the right hip treated by open reduction on a previous admission, May, 1952. During convalescence he developed an ulcer on the right heel which failed to close.

On the present admission, Aug. 23, 1952, he complained of a painful indolent ulcer on the right heel. He gave a history of claudication in the right calf for several years. Findings included an ulcer about 5 cm. in diameter on the point of the right heel covered with a black eschar. All pulses were present in the left lower extremity; no pulses were present below the femoral artery in the right lower extremity.

A. *B.*

Fig. 3.—Case 2. Arteriograms. *A*, Preoperative, three weeks, September, 1952. *B*, Postoperative, October, 1952. (At fifteen months, December, 1953, main channel obliterated, but abundant collaterals established.)

A. *B.*

Fig. 4.—Case 2. Right foot. *A*, Preoperative, September, 1952. *B*, One year postoperative, September, 1953.

On Aug. 26, an arteriogram showed occlusion at the lower one-third of the femoral artery. Small collateral vessels only were visualized distal to the occlusion. A right lumbar sympathectomy and skin graft to the ulcer caused little improvement, and there was complete failure of the graft to take. Further areas of gangrene developed under the compression dressing. These were located on the dorsum and lateral border of the right foot. The patient refused an above-knee amputation, and therefore arterial exploration was advised, a repeat arteriogram having visualized an adequate distal vessel (Fig. 3, *A*).

On Sept. 20, 1952, a thromboendarterectomy was performed, the technique being comparable to that used in Case 1. Anticoagulants were administered for the first two weeks postoperatively.

A palpable popliteal pulse and improved color and temperature of the foot were noted from the time of operation. In one week, a healthy bed of granulations was noted in the ulcer, and the gangrenous areas were much improved. Three weeks after operation an arteriogram showed successful restoration of the lumen of the vessel (Fig. 3, *B*). This progress was maintained, and healing of the ulcer on the heel was complete at four weeks. Pinch grafts placed on the ulcerated areas on the dorsum and lateral border of the foot took completely.

Since discharge from the hospital, the patient has been seen at monthly intervals in the Outpatient Department. On examination in February, 1953, five months postoperatively, the foot was healed, warm, dry, and comfortable. At fifteen months, December, 1953, he managed a fair degree of activity indicated by his two-block uphill walk to the clinic from the streetcar. The popliteal pulse was not palpable. Arteriography revealed that the main channel was blocked, but many collaterals had appeared.

CASE 3.—M. E. (No. 94707), a 66-year-old woman admitted Aug. 14, 1952, complained of claudication of both legs for two years complicated by gangrene of the fifth toe on the right foot appearing one month before admission. There were well-marked changes in both legs, with absence of the pulses distal to the femoral arteries.

The usual measures of bed rest, Buerger's exercises, and right lumbar sympathectomy resulted in no improvement. An additional patch of gangrene appeared on the sole of the right foot. A right femoral arteriogram showed a 7 cm. block at the femoropopliteal junction, immediately adjacent to which were patent vessels with good lumina. The anterior and posterior tibial arteries were apparently occluded, as only profuse fine collaterals were demonstrated in the leg.

An exploration of the femoral artery, the only alternative to an above-knee amputation, was considered worth while and performed on Oct. 30, 1952. Little change occurred in the ischemic foot following the operation, and a check arteriogram revealed extension of the thrombotic process in the femoral artery. Persistent pain and failure of resolution of the gangrenous patches necessitated above-knee amputation approximately one month after the endarterectomy.

CONCLUSIONS

Two patients with segmental occlusion complicating arteriosclerotic disease of the femoral vessels have had limb salvage from thromboendarterectomy. These results remain satisfactory at intervals of eighteen and fifteen months, respectively, a longer period of observation than commonly reported. A third case was a failure due, we feel, to poor selection, there being widespread arterial occlusion evident clinically and arteriographically.

It is submitted that thromboendarterectomy is a feasible surgical procedure to restore arterial patency in cases of segmentally occlusive arteriosclerotic vascular disease. The improvement in vascular supply effected has been maintained for a substantial length of time, proving this to be more than a temporary phenomenon. To select suitable cases, a wider use of arteriographic studies is indicated.

REFERENCES

1. Bazy, L.: L'Endartérectomie pour artérite oblitérante des membres inférieurs, J. internat. chir. **9**: 95, 1949.
2. dos Santos, J. C.: Note sur la désobstruction des thromboses artérielles anciennes, Presse méd. **57**: 544, 1941.

3. Freeman, N. E., and Gilfillan, R. S.: Regional Heparinization After Thromboendarterectomy in the Treatment of Obliterative Arterial Disease, SURGERY **31**: 115, 1952.
4. Julian, O. C., Dye, W. S., Olwin, J. H., and Jordan, P. H.: Direct Surgery of Arteriosclerosis, Ann. Surg. **136**: 459, 1952.
5. Leriche, R., and Kunlin, J.: Essais de désobstruction des artéres thrombosées suivant la technique de Jean Cid dos Santos, Lyon chir. **42**: 675, 1947.
6. Wylie, E. J., Kerr, E., and Davies, O.: Experimental and Clinical Experiences With the Use of Fascia Lata Applied as a Graft About Major Arteries After Thromboendarterectomy and Aneurysmorrhaphy, Surg., Gynec. & Obst. **93**: 257, 1951.
7. Wylie, E. J.: Thromboendarterectomy for Arteriosclerotic Thrombosis of Major Arteries, SURGERY **32**: 275, 1952.
8. Reboul, H., and Huguier, J.: Endarterectomie aortico-iliacque gauche datant de seize mois, Acad. chir. **75**: 318, 1949.

CARCINOMA OF THE CECUM

With Presentation of Two Cases Complicated by Acute Perforation

William L. Martin, M.D., Frank A. Veri, M.D., and
Robert Bower, M.D., Philadelphia, Pa.

(From the Department of Surgery, Hahnemann Medical College and Hospital)

IN THE year 1952, within a period of four days, the senior author had on his service two consecutive cases of carcinoma of the cecum complicated by acute perforation of the lesion. In both cases laparotomy was performed as an emergency procedure, and in both cases it was found necessary to perform a right hemicolectomy in the absence of preoperative preparation of the bowel and in the face of a complicating peritonitis; both patients had uneventful recoveries. The occurrence of these two similar cases in so short an interval prompted us to review the literature on the subject and, subsequently, to report the cases together with the details of management and the immediate results of treatment.

INCIDENCE

Ulin and associates[1] in 1950, in reviewing the cases of colon malignancy for the years 1945-1949 at this hospital, found twenty-four of 342 to be cecal carcinomas, an incidence of 7 per cent. This figure is in agreement with other published statistics.[2]

The incidence of frank perforation among cecal carcinomas is more difficult to ascertain because of a paucity of published data. However, Ransom[3] found four perforations among ninety-one carcinomas of the right colon, an incidence of 4.4 per cent.

ETIOLOGY

The etiology of carcinoma remains unknown. In a consideration of cecal malignancies, however, as with large bowel malignancies in general, the relation of chronic inflammation and pre-existing adenomas to the appearance of carcinoma should be mentioned. Atwater and Bargen,[4] in their review of intestinal polyps, presented evidence of the gradual transition from benign adenomas to frank carcinoma.

Helwig,[5] in a review of 1,460 necropsies, found colonic adenomas in 16 per cent of individuals over 30 years of age and evidence of malignant transition in 7.2 per cent of the adenomas. Also, the high incidence of malignancy in intestinal polyposis lends credence to the supposed relationship between benign adenomas and subsequent carcinomas.

The role of chronic inflammation in the subsequent appearance of carcinoma remains uncertain. It is reported,[6] however, that carcinoma appears in 25 to 30 per cent of long-standing cases of ulcerative colitis, an incidence far above the expected rate of occurrence in the general population. Also, colonic diverticulitis and carcinoma are found together in about 1 per cent of cases.

Bargen and Sauer[7] suggested that the development of malignant lesions in the face of chronic inflammation represents an abnormal uncontrolled phase of the process of healing.

PATHOLOGY

A recent five-year survey of over 3,000 cases of malignancy of the colon at the Mayo Clinic revealed 98.3 per cent to be adenocarcinoma in type, 1.2 per cent epithelioma, and 0.5 per cent malignant lymphoma. Carcinoid tumors or argentaffinoma were found in the colon but were quite rare.

Received for publication, Jan. 11, 1954.

Adenocarcinoma of the colon can be divided into two gross types: papillary and infiltrating or scirrhous. The papillary form projects into the lumen and varies in size from a small elevated wart a few millimeters in diameter to a large fungating cauliflower mass 10 cm. or more in diameter. This type of tumor, which occurs frequently in the cecum and right colon, may be the initiating factor in an intussusception, which in turn may produce obstruction. The infiltrating type of adenocarcinoma is a hard, fibrous tumor that tends to encircle the bowel wall and constrict the lumen. It forms the so-called "napkin-ring" tumor and is usually found in the left colon.

A carcinoma of the cecum may possess characteristics of both these types. Each tumor becomes ulcerated depending upon the degree of impaired circulation due to the rapidity of growth, trauma from intraluminal content, infection, or a combination of these factors.

The average surface area of carcinoma of the cecum is 51.6 sq. cm. compared to 31 for that of the sigmoid. Because of the large caliber of the cecum (7.5 cm. in diameter compared to 2.5 cm. for the sigmoid), the papillary type of tumor, and the liquid consistency of the fecal stream, obstruction of the lumen of the cecum is rare.

The most common site of origin of a cecal carcinoma is opposite the ileocecal valve with spreading around the valve and finally forming of an annular lesion above the lower pole at the level of the valve. The direct extension spread is usually to the lateral gutter, where often the cecum becomes adherent. The lymph nodes most frequently affected are the adjacent intraperitoneal ones, although the peritoneum itself and the liver are frequently the sites of early metastases. Thus, the modes of spread are: (1) direct extension, (2) lymphatics, and (3) the blood stream.

SYMPTOMATOLOGY AND DIAGNOSIS

The clinical picture presented by a patient with carcinoma of the cecum may place him in any one or a combination of the following groups:

Group 1. The Anemic or Debility Group.—Approximately 79 per cent will show less than 13 Gm. of hemoglobin and 54 per cent will show less than 11 Gm. The patient complains of weakness, loss of interest, fatigue, and later will have a loss of weight. In any unexplained anemia, especially in the elderly age group, a possible diagnosis of cecal malignancy should be entertained.

Group 2. The Dyspeptic Group.—Anorexia, bloating, belching, indigestion, and epigastric fullness with nausea may be the presenting complaints. Approximately 20 per cent have vomiting, and a like percentage have diarrhea. Some type of abdominal discomfort such as cramps or severe pain may be present (76 per cent) and may lead one to think of an acute biliary colic or acute appendicitis. Changes in bowel habits may occur, with loose stools being present. On further questioning, however, it will be learned that frequently there is an alteration between loose stools and constipation. Mucus and blood may be present in the stool.

Group 3. A Palpable Mass Without Symptoms.—This may be found on a routine examination or may be first observed by the patient himself.

Group 4. Signs of Acute Abdomen.—Signs of an acute intra-abdominal inflammatory process may arise from an acute appendicitis secondary to a partially obstructing cecal lesion, from inflammatory changes within the cecal tumor mass itself, or from a perforation of the cecal lesion with resulting peritonitis.

Mayo and Lovelace,[8] in reporting their series of carcinomas of the cecum and ascending colon, found that 15 per cent were initially diagnosed as acute appendicitis. In Patterson and Deaver's[9] series, 17 per cent were originally diagnosed as having, and were operated upon for, acute appendicitis, and among those subjected to resection, there were acute inflammatory changes in the appendix in 10 per cent.

Thus, it would appear that in a definite proportion of cecal carcinomas, the initial symptoms arise from a complicating inflammatory process either in the lesion itself or in the adjacent appendix and that occasionally a cecal carcinoma remains unrecognized when the secondarily inflamed appendix is removed.

The cases described in this paper are illustrative of the group presenting as an acute surgical abdomen, although in these cases there was free perforation of the lesion with peritonitis rather than the more commonly observed local inflammation of appendix or cecal wall.

A.

B.

Fig. 1, *A* and *B*.—*A*, View of anterior aspect of cecum in Case 1. Notice the discoloration of the bowel wall and the multiple small perforations at the base of the cecum.

***B*, Cross-sectional view of the lesion, showing the marked narrowing of the lumen of the cecum and impingement on the ileocecal valve.**

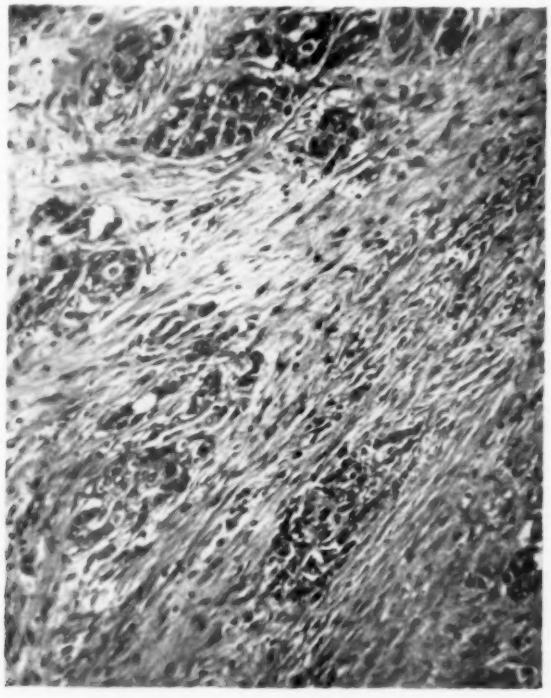
TREATMENT

At the present time, the prognosis in cases of cecal carcinoma is the best of any of the colon malignancies, and reports of five-year survivals of up to 75 per cent have appeared in the literature. The comparatively favorable outlook in this disease is due in large part to the clinical behavior of the tumor, large luminal growths with slow mural penetration and

late lymphatic extension being the rule. Some credit, however, belongs to the currently practiced surgical treatment, including right hemicolectomy and either primary ileocolostomy or exteriorization and subsequent restoration of bowel continuity after the method of Mikulicz. As a cancer operation, this procedure, with its wide removal of all lymph channels draining the affected segment in addition to wide excision of the terminal ileum and proximal colon, probably excels the methods now applicable to other portions of the colon.

The widespread use of the sulfonamides and antibiotics in the control of peritoneal contamination by coliform organisms has rendered less essential the application of the exteriorization principle, although this latter technique maintains a definite sphere of usefulness in the poor-risk patient and in the occasional case where preoperative preparation of the bowel has not been possible.

The two cases reported here, in which resection and primary anastomosis were carried out in the presence of known peritoneal contamination and in which postoperatively there was no evidence of intra-abdominal sepsis, bear witness to the effectiveness of current antibiotics in the prevention and control of potential or existing peritonitis.



C.

Fig. 1, *C.*—Photomicrograph from the lesion in Case 1, showing a Grade II adenocarcinoma.

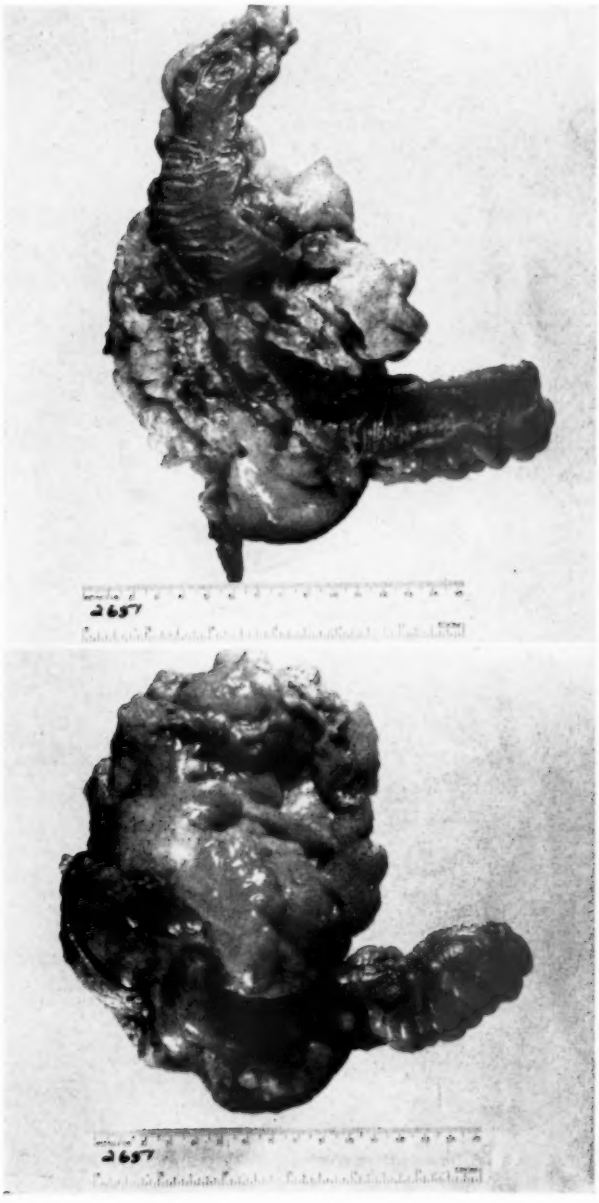
CASE REPORTS

CASE 1.—A 48-year-old white woman was admitted to the hospital eleven hours after the abrupt onset of severe abdominal pain. The pain was at first situated in the right lower quadrant but spread rapidly over the entire abdomen. Vomiting began about one hour after the onset of pain and persisted until admission.

The past history revealed that the patient had been under treatment by her personal physician for a period of about four months because of intermittent, crampy, abdominal pain associated with two or three semiformed bowel movements daily. There was no history of previous vomiting or melena. The patient had also been under treatment for five years for Parkinson's disease.

Physical examination of the patient on admission revealed a thin middle-aged white woman in acute abdominal pain. Examination of the heart and lungs was essentially negative. The abdomen was not distended but showed marked rigidity throughout and marked generalized tenderness which was greatest in the right lower quadrant. There was generalized rebound

A.



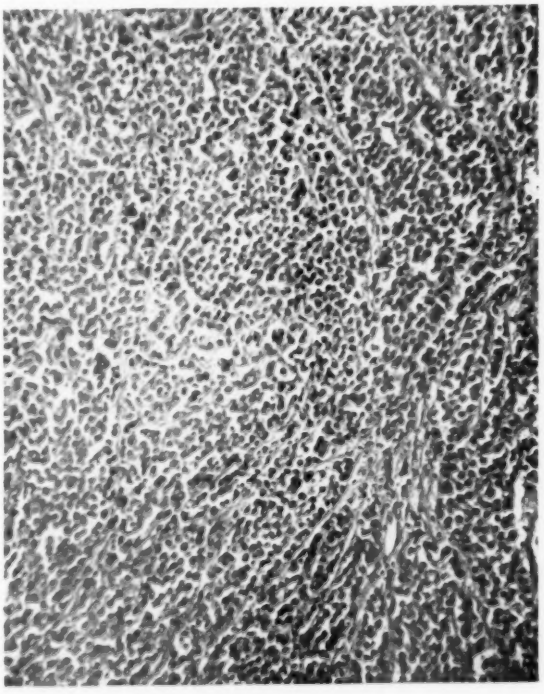
B.

Fig. 2, *A* and *B*.—*A*, Cross section of the cecum in Case 2, showing the polypoid growth which has narrowed the lumen of the cecum.
B, Anterior surface of the cecum, showing the perforation in the cecal wall.

tenderness; a rare peristaltic sound was heard. Pelvic examination revealed only marked tenderness. Rectal examination disclosed normal-appearing feces; no mass or blood was present. A presumptive diagnosis of a perforated viscus with peritonitis was made, and the patient was prepared for surgery.

At operation a large annular infiltrating carcinoma of the cecum was found which was constricting the lumen of the cecum beyond the ileocecal valve (Fig. 1, *B*). On the anterior surface of the cecum was an area about 2 cm. in diameter which was coated with plastic exudate. The entire thickness of the cecal wall in this area was honeycombed with small perforations leading from the serosal surface to an area of necrosis in the tumor on the mucosal surface. Free communication between the lumen of the bowel and the peritoneal cavity existed through these perforations (Fig. 1, *A*). There was approximately 300 c.c. of cloudy, purulent fluid in the peritoneal cavity. The serosal surfaces of the viscera were widely coated with plastic exudate.

The terminal ileum, cecum, ascending colon, and right half of the transverse colon were resected in continuity with the attached mesentery and lymphatics. A primary side-to-side ileotransverse colostomy was then performed. A Penrose drain was placed in the pelvis and the incision was closed in layers. Microscopic examination of the tumor revealed a Grade II adenocarcinoma (Fig. 1, *C*).



C.

Fig. 2, *C*.—Photomicrograph from lesion in Case 2, showing a poorly differentiated carcinoma.

Postoperatively the patient was kept on continuous gastric suction; 100,000 units of penicillin and 0.5 Gm. of streptomycin were administered every six hours; intravenous fluids were given to maintain fluid balance. Suction was discontinued after forty-eight hours and oral feedings were started. The first bowel movement occurred on the fourth postoperative day. On the sixth day the drain was removed, following which there was a transient elevation of temperature. Convalescence was uneventful thereafter, and the patient was discharged on the twelfth postoperative day in good condition.

CASE 2.—A 78-year-old white woman was admitted to the hospital with a history of abdominal pain beginning about three weeks before admission. The pain was situated in the right upper quadrant of the abdomen and was accentuated by moving or coughing; it had no apparent relationship to the ingestion of food or to bowel function. On the day before

hospitalization, the pain suddenly became more severe and was followed by the onset of nausea and vomiting. The past medical history revealed no food intolerances and no change in bowel function.

Physical examination on admission to the medical service showed a temperature of 101.8° F.; the lungs and cardiovascular systems were not remarkable. The abdomen was not distended; there was tenderness to palpation in the right upper abdomen with slight rebound tenderness; a questionable mass was present; peristalsis was markedly hypoactive. A presumptive diagnosis of acute cholecystitis was made.

The day after admission, the senior author was called in consultation. Marked tenderness persisted low in the right upper quadrant with localized rebound tenderness. A scout film of the abdomen showed multiple gall bladder calculi with no abnormal gas patterns. A blood count showed a moderate anemia; blood chemistries were within normal limits. An electrocardiogram was normal. A presumptive diagnosis of acute cholecystitis with possible perforation was made, and the patient was prepared for immediate surgery.

With the patient on the operating table under spinal anesthesia, the abdomen was reexamined, and a definite mass was again palpated which was several centimeters lower than an inflamed gall bladder would commonly be found. The situation of the mass, the previously reported anemia, and the fresh memory of the first case reported here prompted the surgeon to make the incision midway between the costal margin and the iliac crest rather than in the subcostal area.

When the abdomen was opened, a large, fungating carcinoma of the cecum was found involving most of the circumference of the lower cecum in annular fashion and constricting the lumen of the colon (Fig. 2, *A*). On the anterior aspect of the cecum was a 6 mm. perforation in the bowel wall connecting the lumen of the colon with the peritoneal cavity; this was surrounded by plastic exudate (Fig. 2, *B*). The lateral parietes apparently had localized the perforation to some extent, for there was not widespread peritoneal contamination. The terminal ileum, cecum, ascending colon, and right half of the transverse colon were resected in continuity with attached mesentery and lymphatics. A side-to-side ileotransverse colostomy was then carried out. Microscopically the tumor proved to be a poorly differentiated adenocarcinoma (Fig. 2, *C*).

Postoperatively, the patient was placed on continuous gastric suction; 100,000 units of penicillin and 0.5 Gm. of streptomycin were administered every six hours; intravenous fluids were given to maintain fluid balance. After forty-eight hours the Levin tube was removed and fluids were begun orally. The patient developed some abdominal distention, and gastric suction was reinstituted until the fourth postoperative day, at which time it was again withdrawn. The patient's temperature reached a maximum of 100.2° F. on the first postoperative day and was normal thereafter. Flatus was expelled on the second postoperative day, and bowel movements occurred on the fifth. The patient's convalescence was smooth and she was discharged on the fifteenth hospital day.

SUMMARY AND CONCLUSIONS

Two consecutive cases of carcinoma of the cecum are reported which presented clinically as acute surgical abdomens. In each case a large, cecal tumor was found with free perforation of the lesion and concomitant peritonitis. In each case a right hemicolectomy with primary ileocolostomy was performed. Both patients had an uneventful recovery following surgery.

The general subject material of cecal carcinoma is reviewed. Particular attention is drawn to the cecal lesion, which presents primarily as an inflammatory process, either as a secondary appendicitis, as inflammation in the carcinoma itself, or as perforation of the lesion with peritonitis. The need for careful evaluation of the cecum when operating on the acute right lower abdomen in patients in the cancer age group is emphasized.

It is suggested that with the assistance of the antibiotics, even in the presence of peritoneal contamination and without previous bowel preparation, definitive resection of a perforated colon malignancy with primary anastomosis can be carried out as an emergency procedure without undue risk to the patient and with no appreciable increase in postoperative morbidity.

REFERENCES

1. Ulin, A. W., Grotzinger, P. J., Sacks, C. L., and Martin, W. L.: Diagnostic and Therapeutic Problems in Large Bowel Obstruction Due to Carcinoma of the Colon, Pennsylvania M. J. **53**: 1290-1294 (Dec.) 1950.
2. Boehme, E. J., and Hensen, P. J.: Carcinoma of Colon and Rectum: Site of Growth of 1,451 Lesions, S. Clin. North America **26**: 551 (June) 1946.
3. Ransom, H. K.: Carcinoma of the Right Colon, SURGERY **5**: 340, 1939.
4. Atwater, J. S., and Bargen, J. A.: The Pathogenesis of Intestinal Polyps, Gastroenterology **4**: 395, 1945.
5. Helwig, E. B.: The Evolution of Adenomas of the Large Intestines and Their Relation to Carcinoma, Surg., Gynec. & Obst. **84**: 36, 1947.
6. Cattell, R. B., and Boehme, E. J.: Chronic Ulcerative Colitis Complicated by Carcinoma of Colon and Rectum, S. Clin. North America **26**: 641, 1946.
7. Bargen, J. A., and Sauer, W. G.: Association of Chronic Ulcerative Colitis and Carcinoma, Clinics **3**: 516, 1944.
8. Mayo, C. W., and Lovelace, W. R., Jr.: Malignant Lesions of the Cecum and Ascending Colon, Surg., Gynec. & Obst. **72**: 698, 1941.
9. Patterson, J. F., and Deaver, J. M.: Carcinoma of the Cecum, Am. J. Surg. **81**: 6, 618-621 (June) 1951.

SKIN NECROSIS FOLLOWING INTRAVENOUS USE OF NOREPINEPHRINE

Case Reports

Edith R. Kepes, M.D., Henry Haimovici, M.D., and Bernard Simon, M.D.,
New York, N. Y.

(From the Surgical Division, Montefiore Hospital)

Levophed (l-arterenol or norepinephrine) is widely used as a potent vasopressor agent. It is an accepted drug in surgical and medical conditions associated with shocklike states. As it is a relatively new drug, its complications have not been fully evaluated. Thus the following case histories might be useful to shed further light on the occasional complications which follow its intravenous administration. Similar observations have been published by Bergmann,[1] Kurland and Malach,[2] and Uricchio, Calenda, and Cutts.[3]

Case 1.—(M. H., No. 61388R) A 26-year-old white woman was admitted to Montefiore Hospital for mitral commissurotomy. The history revealed repeated episodes of rheumatic activity and multiple episodes of embolization. Preoperative symptoms were two-pillow orthopnea, ankle edema, and paroxysmal nocturnal dyspnea. Physical examination revealed: auricular fibrillation, blood pressure 130/80, pulse rate 76, right ventricular hypertrophy and retrosternal dullness, a loud mitral stenotic sound, a loud pulmonic second sound, a diastolic apical murmur rough Grade 3, also a blowing, basilar systolic Grade 1 murmur. After adequate preparation including digitalization, mitral commissurotomy was performed on Aug. 2, 1953, under nitrous-oxide-ether anesthesia. After the chest was opened, the blood pressure fell to 80/50. Levophed (4 μg per cubic centimeter) was then administered through a 13 gauge Horsley cannula placed preoperatively into the saphenous vein at the level of the left ankle. This brought the blood pressure back to its preoperative level. At the completion of surgery, Levophed was discontinued but restarted six hours later through the same cut down, when the pressure once more dropped to 90/65. This was continued for forty-eight hours.

After this time, a superficial thrombophlebitis was noted, and the Horsley cannula was removed. The following day a large 6 by 3 cm. blister full of amber-colored fluid with smaller blisters 3 by 3 cm. inferiorly was seen on the medial aspect of the left leg, 20 cm. above the ankle. This area proceeded to ulceration and sloughing. Six weeks after the lesion was first seen, the area 13 by 7.5 cm. was removed down to the muscle aponeurosis, and a split-thickness graft, taken from the anterolateral area of the right thigh, was applied successfully.

The histopathologic study of the excised area showed that only small scattered foci of squamous epithelium remained. The bulk of the epithelium had been destroyed. There were focal zones of subepidermal edema in the few zones where epithelium remained. There was massive edema, marked vascular congestion, and a dense, nonsuppurative mononucleated cellular inflammatory infiltrate in the corium and the subjacent tissue. This inflammatory process also involved the subjacent musculature. In the available sections, only a rare small venule in the midst of an inflammatory focus was thrombosed. There was no evidence of extensive or primary venous thrombosis in the available sections.

Case 2.—(M. H., No. 62720) A 75-year-old white man was admitted with the diagnosis of hypersplenism. The history revealed progressive generalized weakness of three months' duration, syncope, and intermittent abdominal discomfort not clearly related to food. He

Received for publication, March 18, 1954.

had had recent tarry stools, sporadic fever 100° to 101° F., with a weight loss of 27 pounds in the previous twelve months. Physical examination revealed: pulse rate 80, blood pressure 116/80, liver three fingerbreadths below the right costal margin, and an enlarged spleen. The main laboratory results showed: hemoglobin 6 Gm., red blood count 2,000,000, hematocrit 22 per cent, reticulocytes 9.3 per cent, bleeding time nine minutes, clotting time nine minutes, coagulation time four minutes, platelets 768,000. Bone marrow puncture showed severe hyperplasia with markedly increased megakaryocytes, many megakaryoblasts; very few were making platelets. A diagnosis of hypersplenism was made. Several transfusions were given, and splenectomy was performed on Oct. 16, 1953. Postoperatively, the patient went into shock due to internal bleeding, was re-explored, the clots evacuated, the bleeding vessels ligated, and blood loss replaced with blood transfusions. His blood pressure remained stable for the following twenty-four hours. On the second postoperative day he developed hypotension with peripheral vascular collapse. In addition to blood transfusions, Levophed (4 μg per cubic centimeter) was started through a 13 gauge Horsley cannula which was placed into the surgically exposed saphenous vein at the level of the right ankle. This was maintained for forty-eight hours.

Fig. 1.—Early lesions of the skin. Note blisters in the necrotic area.

Six hours after Levophed was first started, a purplish mottling of the skin on the medial aspect of the right leg from the knee to the midleg was seen. In the next six hours this area became diffusely purple in color and well demarcated, measuring 15 by 22.5 cm. There was also a blister superiorly and two obvious areas about 3 cm. in diameter where the epidermis had been shed (Fig. 1).

This patient's course was progressively downhill with the development of uremia. He expired on the twelfth postoperative day.

Tissue segments from this necrotic area obtained at post-mortem showed essentially similar lesions to those in Case 1.

CASE 3.—(M. H., No. 63009) A 66-year-old white man was admitted to Montefiore Hospital on March 20, 1953, because of urinary retention. The past history was noncontributory. On physical examination a benign prostatic hypertrophy was found. Review of his systems was negative, except for a slightly enlarged heart with Grade 2 systolic murmur in the aortic area and an arterial blood pressure of 170/100. An electrocardiogram showed evidence of old anterior wall damage. The peripheral circulation was normal.

On April 1, 1953, a suprapubic prostatectomy was performed. Twenty-four hours after operation, the patient went into mild shock and was successfully treated with a transfusion of 500 c.c. of blood and an infusion of Levophed (4 μg per cubic centimeter). One month

later, on May 5, 1953, the patient suddenly developed a shocklike condition associated with a temperature of 106° F. and a fall in blood pressure to 100/60 with a pulse rate of 130. The nature of this shock was not quite clear, although it appeared that the most likely explanation for the hyperpyrexia was related to a bacteremia associated with a genitourinary infection. In addition to oxygen and morphine sulfate, 1/6 grain, Levophed, 4 μg dissolved in 1,000 c.c. of 5 per cent dextrose in water, was administered at a rate of 60 drops per minute. The infusion was given via a polyethylene tube introduced through a cut down above the right ankle into the long saphenous vein. Despite the Levophed, the blood pressure could not be maintained satisfactorily for several hours. Neosynephrine, 0.5 c.c., was then added to the infusion. At 12:30 A.M. the patient was still restless, the temperature was 103° F., and the blood pressure rose to 110/70. During the following three days the patient vomited coffee-ground material several times. His blood pressure was maintained at around 100/60 with Levophed and Neosynephrine. A right acute suppurative orchitis was diagnosed on the fourth day. Phlebitis of the right saphenous vein, without calf tenderness or Homans' sign, was also noted. An orchidectomy was performed the same day. Because of occasional precipitous falls of blood pressure, the Levophed infusion was continued through the left saphenous vein. On the second postoperative day, a gangrenous area appeared in the medial aspect, upper half of the left leg, along the course of the long saphenous vein. The infusion was discontinued. The gangrene was superficial and measured 9 cm. by 3 cm. (Fig. 2). There was moderate pitting edema of the leg. Both foot pulses were normal. The color and temperature of the skin of the foot and leg were also normal. The lesion was treated conservatively by local dressings with a bland ointment. The lesion demarcated and separated away spontaneously after two months. Complete healing of the ulcer occurred within three weeks, and the patient was discharged ambulatory with the leg in good condition.

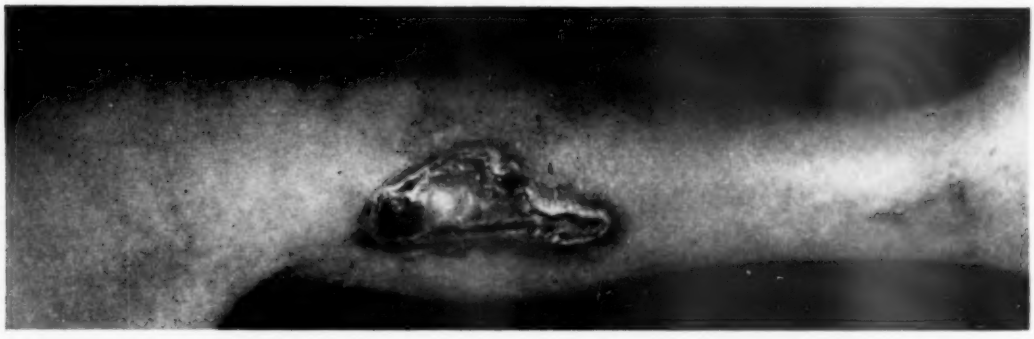


Fig. 2.—Later stage of the necrosis with separation from the normal skin. Note distance between cut down at the ankle and the area of necrosis.

COMMENT

Skin necrosis following accidental extravasation during Levophed infusion reported by others and also observed by us is due to direct and prolonged action of the drug on the vascular bed. This type of skin gangrene is mentioned here only for the purpose of differentiating it from lesions induced by strictly intravenous infusion.

In the three cases reported here, accidental local extravasation was prevented by using an indwelling catheter or Horsley cannula. In spite of this precaution, tissue necrosis with ulceration developed close to the area of the knee. Uricchio and associates[3] expressed the opinion that occlusive vascular disease in the lower leg may be responsible for this complication, while Bergmann[1] advocated the theory that because of the lowered venous pressure in shock, a reflux of norepinephrine occurs into the collateral venules.

The localized necrosis of the skin may occur either as a result of massive venous thrombosis associated with marked arteriolar spasm or because of marked and prolonged arteriolar-capillary spasm. When gangrene occurs due to venous occlusion, as reported by one of us,[4] this is seen only after extensive thrombosis of both deep and superficial veins. In the present group of cases, as well as in those reported in the literature, there is no such evidence.

A marked arteriolar-capillary spasm as a result of prolonged administration of Levophed seems to offer a more satisfactory explanation of the skin necrosis. The patients who developed superficial gangrene following intravenous infusion of Levophed were so treated because of profound peripheral vascular collapse. In such cases, there is evidence of slowdown of the peripheral circulation. The hydrostatic pressure of the infusion fluid containing Levophed is of sufficient force to push the drug a considerable distance from the ankle. This pressor amine, which is a potent vasoconstrictor, causes sufficient narrowing of local veins, so that at the level of the knee, circulation is further slowed down. This may reach such a degree that stagnation of Levophed occurs. In this area a reflux into the collateral venules may take place, reaching the capillaries and arterioles. Constriction of these vessels then leads to a profound local ischemia, which in turn is followed by tissue necrosis.

From a therapeutic standpoint, although most of the ulcers reported healed spontaneously after the discontinuation of the Levophed infusion, one of our cases, one of Bergmann's,[1] as well as one of Kurland and Malach's[2] required skin grafting to repair the damage. As suggested by Kurland and Malach, the application of hot packs at and above the level of the needle may be a valuable procedure in the prophylaxis of the local ischemia. The potential hazards of the drug exerted locally might well indicate the discontinuation of the use of the veins of the lower extremity as the portal of entry for the administration of Levophed, and should be discarded altogether in the presence of peripheral obstructive arterial disease.

SUMMARY

1. Three cases of skin necrosis following infusion of Levophed without extravasation are reported.

2. Necrosis of skin and subcutaneous tissue occurred at some distance above the point at which the cannula was introduced into the vein.

3. The possibility of skin necrosis when Levophed is infused at the ankle should always be borne in mind.

4. A possible mechanism to explain this complication has been offered.

REFERENCES

1. Bergmann, H.: Advantages and Disadvantages of Prolonged Use of Nor-Epinephrine, Internat. J. Anesthesia **1**: 29-34, 1953.
2. Kurland, G. S., and Malach, M.: The Clinical Use of Nor-Epinephrine in the Treatment of Shock Accompanying Myocardial Infarction and Other Conditions, New England J. Med. **247**: 383-389, 1952.
3. Uricchio, J. F., Calenda, D. G., and Cutts, F. B.: Ulceration of the Skin Following Intravenous Use of Arterenol, J. A. M. A. **152**: 607-608, 1953.
4. Haimovici, H.: Gangrene of the Extremities of Venous Origin, Circulation **1**: 225-240, 1950.

SPONTANEOUS RUPTURE OF THE ESOPHAGUS

Report of a Case Occurring Five Years After Gastric Resection

Anthony V. Migliaccio, M.D., Thomas Forsythe, M.D., and
Charles Cavanaugh, M.D., Providence, R. I.

THE syndrome of spontaneous rupture of the esophagus has been known to the medical profession for over 200 years.[1] Until ten years ago it was regarded as a universally fatal medical curiosity. Diagnosis in all but two of the thirty-five cases reported up to that time was made at autopsy. In 1944, Collis,[2] a British surgeon, reported a case in which he made the correct diagnosis and attempted surgical repair of the rupture. Unfortunately, his patient died. Collis stressed the fact that the preoperative diagnosis should not be difficult if the condition is kept in mind. Because the disease was 100 per cent fatal if treated conservatively, he urged further attempts at surgical intervention. Since that time, reported cases have increased over threefold, indicating that the syndrome is more common than one supposed. Several surgically treated survivals are recorded.[3-5] All recent authors agree that the condition represents an acute surgical emergency and that delay of even a few hours commonly results in death.

Esophageal rupture occurs most commonly in the left posterolateral portion of that organ just above the diaphragm, a proved anatomic weak spot. The stomach is a large muscular receptacle capable of suddenly ejecting great quantities of its contents into the relatively narrow lower esophagus. At times the sudden pressure is sufficient to cause rupture. Thus, most cases occur after a heavy meal during the act of vomiting. We have been unable to find a reported instance of this catastrophe in a patient who has previously submitted to an adequate gastric resection.

CASE REPORT

J. C. (Rhode Island Hospital, No. 520191), a 55-year-old white man, was admitted to the hospital on Nov. 22, 1953, at 10:30 in the evening. Four hours prior to admission, he had eaten a large steak dinner. One-half hour later he experienced sudden nausea and vomited, first food and then about three cupsful of bright red blood. During the emesis he was seized by severe mid-epigastric pain which soon radiated around the left costal margin to his back and left shoulder. The pain was agonizing and aggravated by motion of any kind.

The past history was significant in that in May, 1948, a subtotal gastrectomy was performed for intractable duodenal ulcer. Approximately 80 per cent of the stomach was removed. Recovery was uneventful and, except for rare bouts of heartburn, the patient was asymptomatic until the onset of the present illness. The patient drank rather heavily and adhered to no medical regimen during that time.

Physical examination on admission revealed a very pale man, writhing in pain. The temperature was 97.6° F. by mouth, pulse 96, respirations 30, and blood pressure 110/70. No crepitus of the soft tissues of the neck was detected. The left dome of the diaphragm

Received for publication, March 18, 1954.

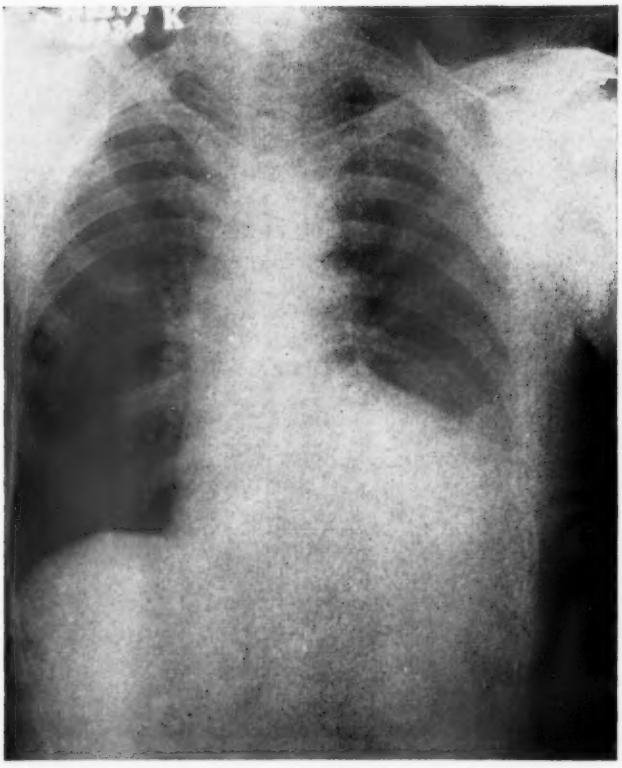


Fig. 1.—Chest film on admission showing moderate pleural effusion with a small collection of air in basal portion of left hemithorax.

Fig. 2.

Fig. 3.

Figs. 2 and 3.—(Barium swallow ten hours after admission.) Oblique (Fig. 2) and lateral (Fig. 3) films showing extensive mediastinal extravasation of opaque material from the site of esophageal rupture just above the diaphragm. It is interesting to note that no leakage of barium into the pleural cavity occurred. There has been moderate increase in the amount of pleural effusion since the initial film.

seemed elevated to percussion and auscultation, but no râles were heard. The upper abdomen was tender and rigid; the lower abdomen was soft and nontender. Peristalsis was present, and normal liver dullness was percussed.

The serum amylase and hemoglobin were normal. White blood count was 13,750 with 54 per cent polys. Flat and upright films of the abdomen showed no significant abnormalities. A posterior-anterior film of the chest showed some fluid at the left base which was not recognized. There was no evidence of mediastinal air or pneumothorax.

The diagnosis of spontaneous rupture of the esophagus was considered in the Accident Room, but it was felt that, in the absence of mediastinal air and crepitus of the neck soft tissues, this was unlikely. The patient was treated conservatively during the night. When seen the following morning, his condition had deteriorated considerably. His pulse was 100 and thready; blood pressure 90/70; skin was cool and had a cyanotic hue. Crepitus of the soft tissues of the neck could be felt. An emergency barium swallow established the diagnosis of ruptured esophagus. A left hydropneumothorax was also evident at this time.

Fig. 4.

Figs. 4 and 5.—Postoperative barium swallow shows a smooth and intact lower esophagus at the site of closure.

Immediately following this procedure, a left thoracotomy was performed, approximately sixteen hours after the onset of symptoms. About 2 L. of dark green fluid and food particles was aspirated from the pleural cavity. A distended mediastinum then became apparent, which, when opened, contained similar material. Both the pleural cavity and mediastinum were irrigated with copious amounts of saline solution. The esophagus was then examined, and a 6 to 7 cm. longitudinal tear was found on its posterolateral aspect just above the diaphragm. This was closed in two layers with interrupted silk. The chest and mediastinum were drained with catheters, and the incision was closed. The patient tolerated the surgery surprisingly well, and at its conclusion, his color had markedly improved.

The next day he was sitting up in bed, free of pain and asking for something to eat. The left lung had completely re-expanded. A Levin tube was kept on suction for three days. On the fourth day this was removed and fluids were allowed. By the seventh day he was on a bland diet. Antibiotics were administered and chest drainage maintained for eleven days because of a low-grade fever. Gastric analysis made during convalescence showed no free hydrochloric acid before or after histamine. A barium swallow performed two weeks postoperatively showed only minimal deformity of the esophagus at the site of surgery. There was no obstruction at this level or at the gastroenterostomy. Approximately 20 per cent of the stomach remained.

Because of his living conditions, it was felt advisable to keep the patient in the hospital longer than would ordinarily have been considered necessary. He was discharged on the twentieth postoperative day. When seen two months after discharge, the patient stated that he felt well and had gained 5 pounds in weight.

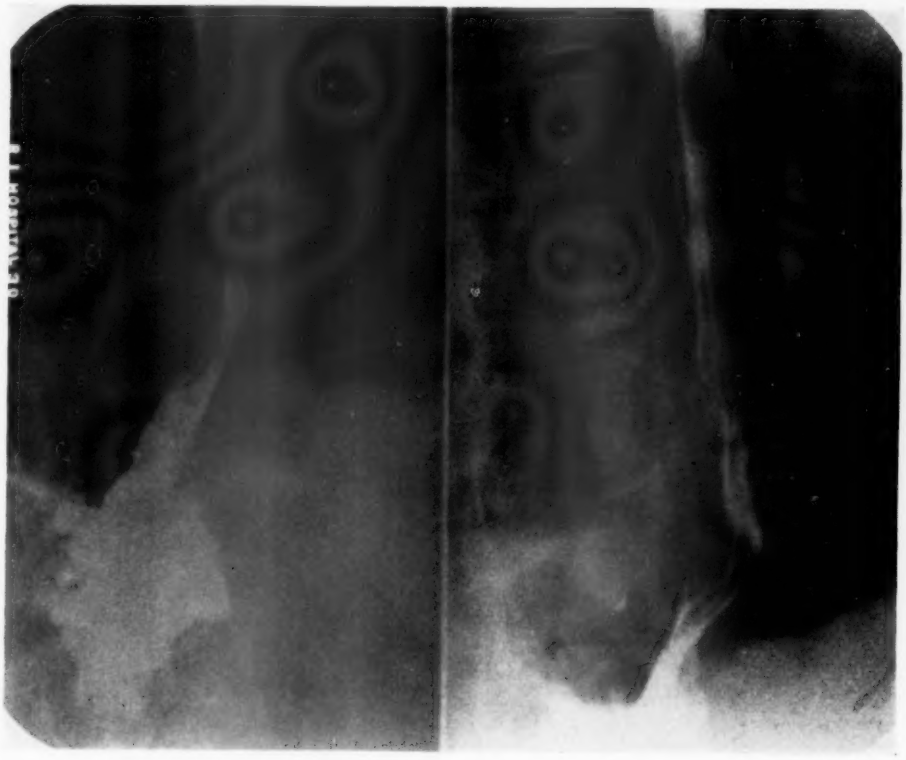


Fig. 5. *(For legend, see opposite page.)*

DISCUSSION

We felt that this case was significant and worth reporting for the following reasons:

1. The case demonstrates that a 20 per cent gastric remnant is capable of exerting sufficient back pressure to cause esophageal rupture.

2. Some authors state categorically that spontaneous rupture of a normal esophagus does not occur.[6] They feel that weakening of the wall, due to pre-existing acid peptic esophagitis, is the sine qua non of the syndrome.

The patient discussed here had an adequate subtotal gastrectomy five years prior to esophageal rupture. Only 20 per cent of the stomach remains. Gastric analysis revealed no free hydrochloric acid before or after histamine. In our opinion, an acid peptic esophagitis seems quite unlikely in this man.

REFERENCES

1. Boerhaave, H.: Atrocia, nec descripti prius, Morbi Historia, Secundum Artia Leges Conscripta, Ludg. Patav., 1724.
2. Collis, J. L., Humphreys, D. R., and Bond, W. H.: Lancet 2: 179, 1944.
3. Kinsells, T. J., Morse, R. W., and Hertzog, A. J.: J. Thoracic Surg. 17: 613, 1948.
4. Lynch, J. P.: New England J. Med. 241: 395, 1949.
5. Samson, P. C.: Surg., Gynec. & Obst. 93: 221, 1951.
6. Wangensteen, O. H.: Discussion, J. Thoracic Surg. 24: 386, 1952.

Editorial

Reply to Dr. Koontz

THE recent editorial on "Surgical Anesthesia" by Dr. Amos R. Koontz cannot go unchallenged by the anesthesiologists. I am sure that the things he speaks of are not general complaints by all surgeons but perhaps arise through special local circumstances in the administration of anesthesia. I doubt that the well-trained and experienced anesthesiologist would lose sight of the forest for the trees in his endeavor to minimize undesirable anesthetic drug side actions, at the expense of surgical facility or patient welfare. Our primary functions as a specialty are to bring patients safely through operation, to facilitate the manipulations of the surgeons, and to minimize or prevent postoperative complications attributable to anesthesia.

With these thoughts in mind, it is inconceivable that many patients will be carried lightly to the point of straining with handicap to the work of the surgeon. We have been compromised by surgeons, patients, and lawyers in our choice of agents today to the point where we may generally use just "garbage" anesthesia (that is, thiopental sodium, nitrous oxide, relaxant, and Demerol). In the good old days, operations were performed under ether given by untrained men with considerable success and without the relaxation we can produce today with a variety of relaxants. Spinal anesthesia was and remains an ideal anesthetic technique for surgery that requires profound relaxation. Cyclopropane is still an excellent agent, but hospital administrators and state fire marshals alike dread its explosiveness; many surgeons but not most anesthesiologists believe that it permits more oozing from the operative field. There are too few reliable signs that the patient is sufficiently deep under "garbage" anesthesia, including the one present when the surgeon says that the patient is straining or when other reflex responses arise. Unfortunately, the better the relaxation from neuromuscular blocking drugs, the more the surgeons expect of us. Some surgeons begin to object the moment spontaneous respiration resumes after an apneic dose of relaxant, no matter how feeble it may be. They confuse movements of the diaphragm from above with the active expiratory function of the muscles of the abdominal wall, which is absent in deep curarization. Our problem is made more difficult by the evident lack of gentleness in the art of intra-abdominal manual exploration and manipulation by most surgeons, for roughness begets reflex protests by the anesthetized patient. Residual curarization at the end of operation because of rapid closure or excessive doses of relaxant to satisfy the surgeon predisposes the patient to postoperative atelectasis, respiratory obstruction with asphyxia, coronary and cerebral vascular accidents, self-narcosis from carbon dioxide accumulation, postanesthetic hypotension, and oliguria.

Dr. Koontz noted that "it is probable that a great many inguinal hernias recur before the patient is out of the anesthetic, when injudicious struggling is allowed" or that postoperative hernias start during unconscious struggling while the patient is under the influence of the anesthetic agent. I can remember an autopsy that showed the start of such a hernia beginning with dehiscence of the peritoneum on a patient who had been given open-drop ether. It is not necessarily the struggling that causes the sutures to break or tear through the peritoneum and fascia, for unnatural relaxation of the abdominal muscles generally exists during surgery, whether due to relaxants, deep anesthesia, or spinal anesthesia. Many patients in full possession of their faculties at the time recall the cough to loosen a bronchial mucus plug that started an incisional hernia. The mucus may have been there because of earlier excessive curarization. The anesthetic struggling is less likely to occur during the awakening if small amounts of narcotics or trichlorethylene are used as anesthetic supplements during surgery in place of the ever-present and often misused thiopental sodium.

By the use of narcotic supplements during anesthesia, the patients are more likely to awaken promptly and yet retain sufficient analgesia to avoid the unconscious struggling noted by Dr. Koontz. Care must be taken in the size of the doses used during surgery and particularly the first postanesthetic dose. Deaths from respiratory depression have followed the use of the routine dose of morphine sulfate 1/6 grain or of Demerol 100 mg. just following surgery.

I have said nothing about the respiratory depressing action of all our drugs except ether and spinals. Aside from favoring the development of atelectasis during and following surgery, respiratory acidosis is generally the rule during surgical anesthesia, with its attendant tendency for increased bleeding, postanesthetic shock, potentiation of anesthetics by the narcotic properties of carbon dioxide excess, and development of cardiac arrest by ventricular asystole or fibrillation. If we employ assisted or controlled respiration, the stomach may become distended with anesthetic gases. If we intubate the trachea, the cough that follows its removal serves to clear mucus from the tracheobronchial tree but at the same time puts a strain on the surgeon's handiwork. We anesthesiologists are in a position where we are damned if we do not and damned if we do. The answer lies in a return when indicated to the use of earlier anesthetic agents and combinations displaced by the ubiquitous "garbage" so popular today. Dr. Koontz must do his best work under ether or spinal anesthesia.

—*Willis G. Watrous*

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

ELECTRICAL TREATMENT OF CARDIAC ARREST: A CARDIAC STIMULATOR-DEFIBRILLATOR

J. A. HOPPS, B.Sc.E.E.,* AND W. G. BIGELOW, M.D., TORONTO, ONTARIO

(From the Department of Surgery, University of Toronto, and the Banting Institute)

THE term "cardiac arrest" is used commonly to include both ventricular fibrillation and cardiac standstill. In both instances there is an "arrest" of normal cardiac function, and the circulation of blood ceases. A heart in standstill may start beating spontaneously, especially with the aid of cardiac massage. Repetitive electric stimuli have proved successful experimentally in producing a return of normal heartbeats. Ventricular fibrillation, on the other hand, must first be converted to standstill, which may be a transient stage, before normal heart action can be restored. Defibrillation is accomplished usually by electric shock treatment.

The purpose of this article is to describe the construction, function, and operation details of an instrument which combines, in one, both a countershock defibrillator and pacemaker stimulator. A closed-chest method of defibrillation is also presented.

The stimulus to pursue the problem of cardiac arrest came from our experimental study of hypothermia as applied to experimental cardiac surgery.[1] Ventricular fibrillation and cardiac standstill are commonly encountered at low body temperatures.

During the last four years, the technique of electric defibrillation in dogs was studied, and an artificial pacemaker was developed for restoration of beats in standstill of the heart. These techniques have been used experimentally at normal body temperature, and the electric circuits continuously modified until satisfactory performance was achieved. It was considered timely, therefore, to offer a description of the equipment and procedure used.

No attempt is made in this article to discuss the technique of cardiac massage, its relationship to electric shock and stimulation, or use of intracardiac injections. This will be included in another communication.[2]

CARDIAC STANDSTILL

Cardiac standstill may occur at low body temperatures. In early experiments it was found that although the heart was in standstill, it would respond

This investigation was supported by a grant from the Defence Research Board of Canada and was carried out in cooperation with the National Research Council of Canada.

Received for publication Dec. 23, 1953.

*Research assistant, Department of Surgery, University of Toronto, and assistant research officer, Radio and Electrical Engineering Division, National Research Council Laboratories, Ottawa, Ontario.

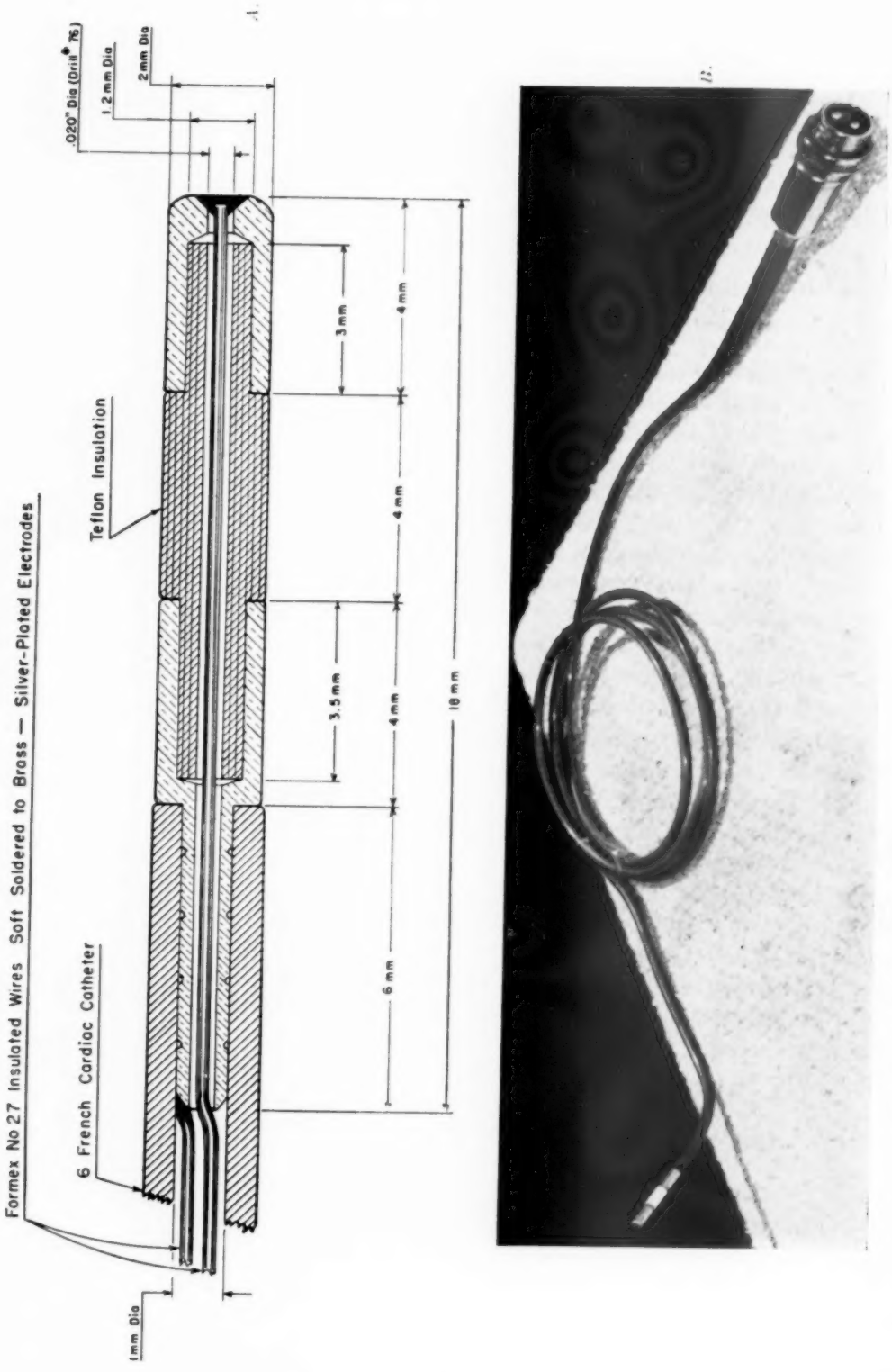


Fig. 1.—A, Construction detail of catheter electrodes. *B*, View of catheter electrodes.

with a vigorous expulsive beat following mechanical stimulation of the auricle or ventricle. This led to experiments which resulted in the development of an electric artificial pacemaker[3] that successfully restored the heartbeat and blood pressure in cases of cardiac standstill at low body temperatures. It was further found that when this stimulator was applied to the sinoauricular (S-A) node area of an animal at normal body temperature and with a normally beating heart, it would "take over" the pacemaker duties and allow one to increase or decrease the heart rate within limits.

The S-A node may be electrically stimulated in various ways. In our first heart stimulation experiments, the stimuli were applied to the pacemaker externally, through the open chest. A small electrode at the tip of an insulated rod was placed at the pacemaker site, with a dispersive electrode on the chest wall. Later an improved technique used two ring electrodes on the insulated rod or two parallel point electrodes, eliminating the dispersive electrode.

Another method of application involves the use of ring electrodes mounted at the end of a cardiac catheter which carries the lead wires. This is inserted into a vein (jugular or arm), and passed along until the tip is in the superior vena cava at the level of the S-A node.

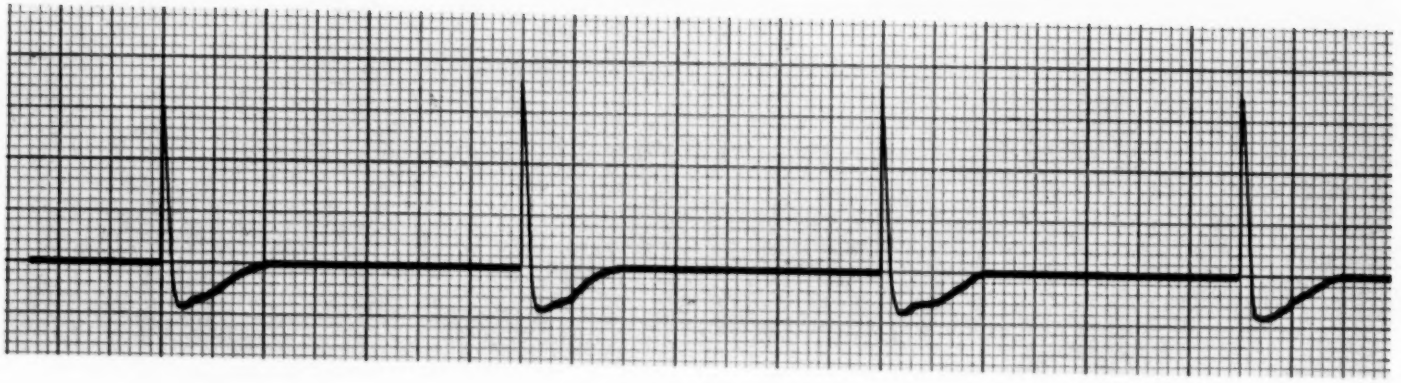
Various arrangements of electrodes have been used on catheters. Fig. 1 illustrates the construction and shows a typical catheter for use in animal experiments. For human application, the electrode spacing can be doubled and the catheter diameter increased to 3 mm.

Pulse Characteristics for Pacemaker Stimulation.—The electric stimulus applied to the S-A node triggers the auricular contraction. Observed on the electrocardiogram it is the P wave of the artificially incited beat. It must be of short duration, or it may blank the portion of the beat corresponding to the QRS complex. The pulse current must be low, or ventricular fibrillation may result. If the pulse is a sequence of sine waves or square waves, it may initiate a beat and then persist to incite ventricular fibrillation during the vulnerable period of late systole.

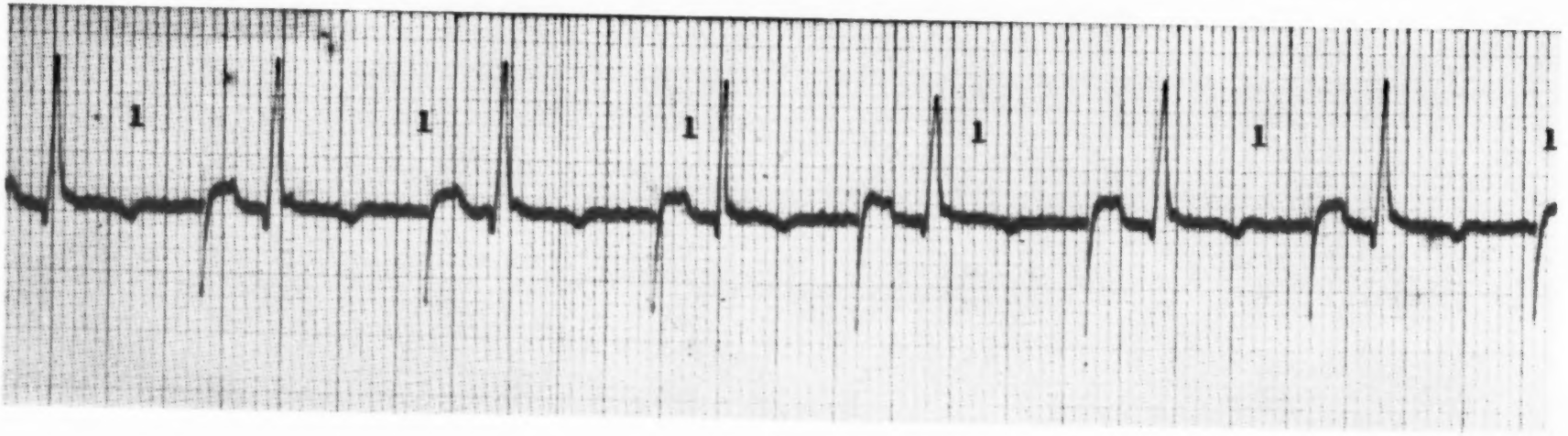
A pulse which has a sharp-rise wave front and a three or four millisecond width simulates the normal P wave fairly well, although its amplitude may be many times that recorded for a normal beat. An exponential decay pulse fulfills the requirement admirably, and is easily produced using a simple thyratron oscillator circuit. The wave form of this type of pulse is illustrated in Fig. 2, *A*.

In our experimental investigations, we have tried other types of stimuli. A biphasic pulse of short duration produced forceful heartbeats but required greater amplitude. Short bursts of sine waves or square waves of various frequencies were unsatisfactory for reactivating a heart in standstill and incapable of controlling a beating heart. In addition, the multiple pulses introduced the danger of ventricular fibrillation.

The polarity of the stimulating pulse had no apparent significance in our tests. Fig. 2, *B* illustrates negative-going stimuli producing inverted "P waves" on the electrocardiogram record.



A.



B.

Fig. 2.—*A*, Stimulator output pulses. *B*, Negative pulses controlling heart rate.

The current required for pacemaker stimulation is difficult to assess. The resistance of the current path between the two electrodes on an intracardiac catheter may vary from 300 to 3,000 ohms depending upon its location. In most instances we have used currents of the order of 10 to 20 Ma. to control heartbeats. Currents as high as 100 Ma. have been used, without observed injurious effect.

The Pacemaker Stimulator.—The stimulator is basically a very low-frequency pulse generator. Pulses from a thyratron oscillator are fed to a cathode-follower output stage. The frequency of the pulses and the voltage amplitude of the output are variable. Frequency is calibrated in terms of heartbeats per minute over a range covering normal requirements.

A circuit for a pacemaker stimulator is shown in Fig. 3. A switch permits connection of external equipment to the electrodes, allowing an impedance check without disconnecting the electrode leads. The stimulating pulse has a sharp rise and exponential decay, with a duration of two to three milliseconds to 67 per cent decay, independent of frequency or voltage amplitude. The pulse may be differentiated to a biphasic form. The pulse rate is variable from thirty to 180 pulses per minute.

Technique of Pacemaker Stimulation.—In practice, there is considerable latitude in positioning the electrodes, as stimuli will excite the node when the electrodes are within three-fourths inch of the nodal area. An open chest allows direct application of the electrode to the S-A node, and it will also make it easy to position an intravenous electrode. If an intravenous electrode is being passed when the chest is not open, its position is determined by measurement and by noting the position in which pulses appear on the electrocardiogram.

The electrodes are connected to the pulse generator with the voltage output turned to 0, and the pulse rate set at the required heart rate. The voltage is then raised slowly. If the electrodes are in proximity to the pacemaker, the pulse should appear on the electrocardiograph. If inserted too far, they may cause diaphragm contraction. When the pulses are evidenced, rate and voltage are adjusted to control the heart action. Fig. 4 illustrates electrocardiograms before, during, and following stimulation of the heart of a dog, in hypothermia with idioventricular rhythm, in which normal heart action was restored.

When pacemaker stimulation is used to reactivate a heart from standstill, it is necessary that the heart be well oxygenated by cardiac massage. The controlled heart will maintain blood pressure at a level comparable with normal action. Stimulation should be stopped periodically to observe whether the normal nodal rhythm has been re-established.

When the pacemaker is applied to a normally beating heart, the artificial stimuli may inhibit normal rhythm, producing beats at the stimulation rate. Artificial stimulation is effective in most cases from about 85 to 150 per cent of the natural rate. Usually it is more effective above the normal rate.

Fig. 2.—*A*, Stimulator output pulses. *B*, Negative pulses controlling heart rate.

VENTRICULAR FIBRILLATION

Ventricular Muscle Action.—Ventricular excitation commences when the contraction of auricular muscle reaches the atrioventricular (A-V) node. The

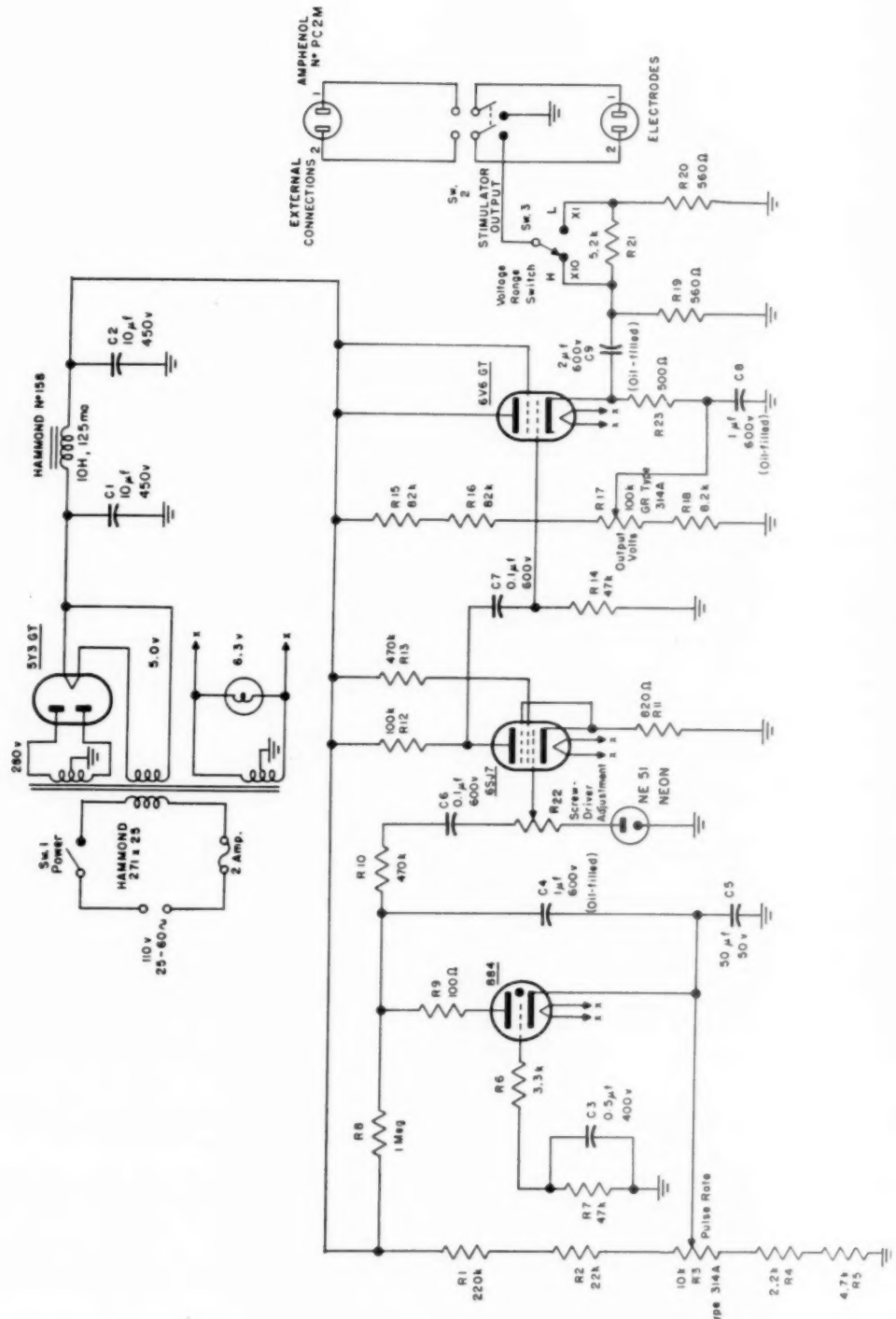


FIG. 3.—A basic pacemaker stimulator circuit.

auricular stimulus is propagated from the A-V node through the bundle of His and branches, to the Purkinje tissue. Like other muscle, ventricular muscle is composed of long, thin fibers which contract if not restrained. The restraint

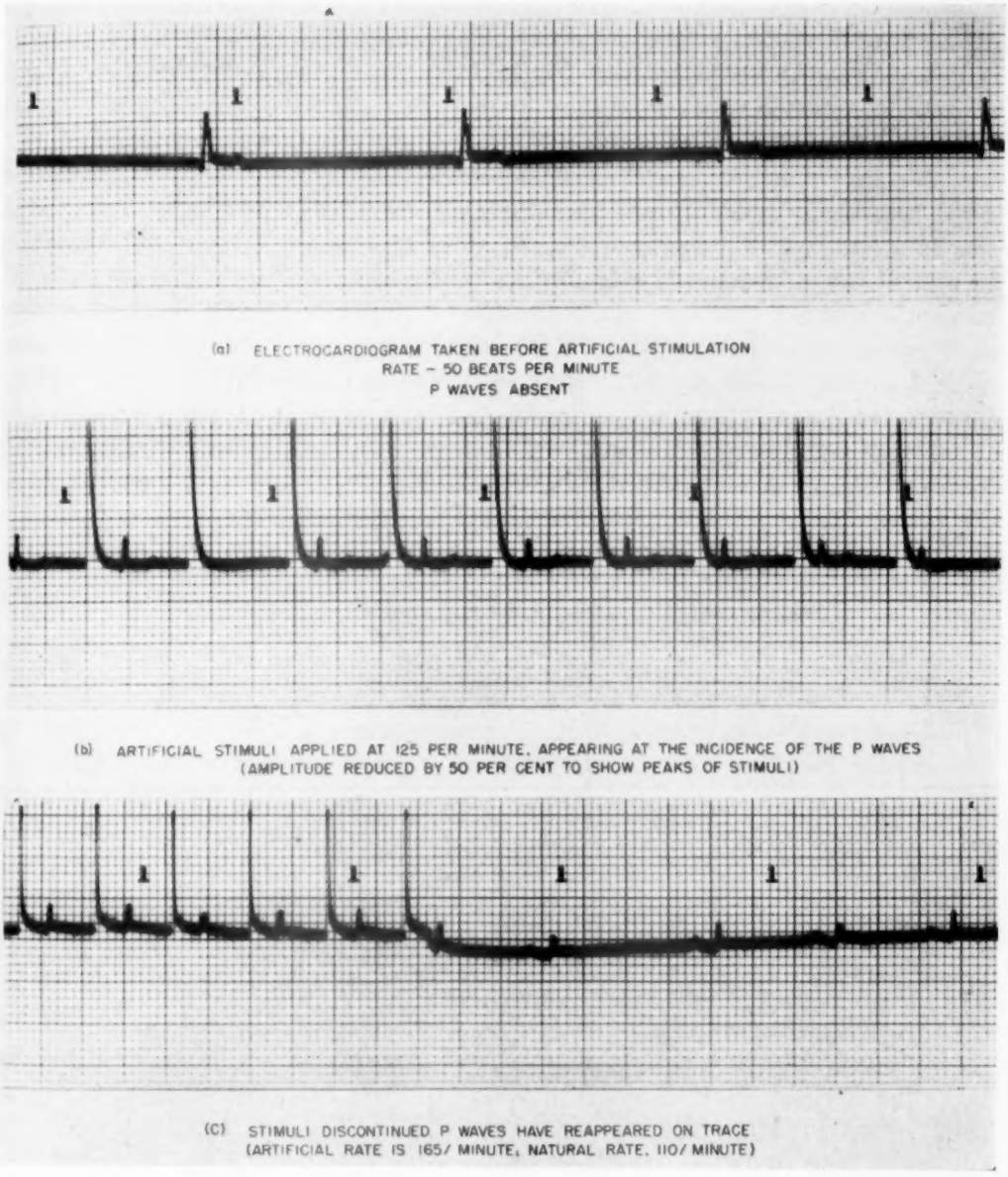

(a) ELECTROCARDIOGRAM TAKEN BEFORE ARTIFICIAL STIMULATION
RATE – 50 BEATS PER MINUTE
P WAVES ABSENT
(b) ARTIFICIAL STIMULI APPLIED AT 125 PER MINUTE, APPEARING AT THE INCIDENCE OF THE P WAVES
(AMPLITUDE REDUCED BY 50 PER CENT TO SHOW PEAKS OF STIMULI)
(C) STIMULI DISCONTINUED P WAVES HAVE REAPPEARED ON TRACE
(ARTIFICIAL RATE IS 165/ MINUTE, NATURAL RATE, 110/ MINUTE)

Fig. 4.—Electrocardiograms recorded before, during, and following stimulation of a dog in hypothermia.

is in the form of electric charges which repel opposite ends of the fibers. Szent-Gyorgyi[4] has pointed out that contraction of the muscle is a depolarization of its constituent fibers.

Ventricular muscle contracts according to the all-or-nothing law, which states that a fiber does not contract by degrees, either contracting fully or not

at all. The muscle action, then, is a function of the number of fibers progressively excited. The summation of the potentials of the fibers at the peak of contraction produces the T wave of the electrocardiogram.

Fibrillation.—If the sequence of fiber excitation is disturbed, there follows a disorganized contraction of fibers throughout the ventricular muscle, and the useful output ceases. There is no period when the fibers are all relaxed; hence the electrocardiogram presents a picture of continuous random activity. This is ventricular fibrillation. In human beings, as in most of the larger animals, it usually is not reversible spontaneously and leads to death from anoxia.

The Principle of Countershock Defibrillation.—The principle was first outlined by Hooker and associates[5] and Wiggers,[6] and the first recorded defibrillation in a human being was described by Beck and Mautz.[7] As stated, the order or progression of the impulse from fiber to fiber in the Purkinje network determines the character of the ventricular beat. In fibrillation the control of fiber activity has been decentralized. If a depolarizing current is applied to each individual fiber simultaneously, there will follow a complete contraction. When the current ceases, the fibers will relax, and the ventricles will then be ready to contract as a unit and thus establish a normal beat. Occasionally defibrillation leaves the heart in standstill.

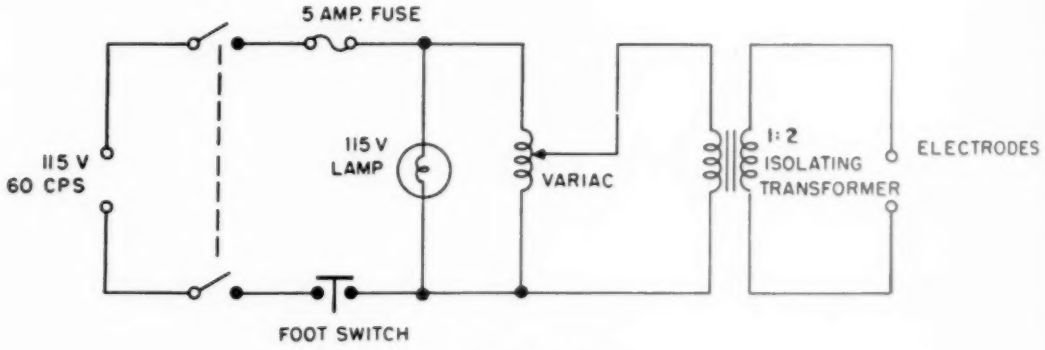


Fig. 5.—A simple defibrillator circuit.

The Countershock Defibrillator.—A simplified defibrillation circuit is shown in Fig. 5. A foot switch controls shock application. Output voltage and hence current are adjusted by a Variac, connected to a transformer which doubles the voltage and isolates both electrodes from ground, for protection of the operator. The electrodes are concaved silver-plated disks on insulated handles. Gauze pads soaked in saline solution can be attached to improve contact between the electrodes and ventricles, although dipping the electrodes alone in saline solution usually assures adequate contact. Details of electrode design are shown in Fig. 6. After assembly, the Bakelite handles are covered with molded rubber grips, sealed to the lead wires. The electrodes may be placed in a sterilizer or autoclave.

A useful addition to the simple defibrillator is a timing circuit for limiting the duration of shock. However, such a feature requires either timer relays or an electronic timer, and is not an absolute necessity in a basic instrument for stand-by use.

The defibrillating shock is applied with the two defibrillator electrodes placed on either side of the heart, after cardiac massage has assured adequate oxygenation. A single shock of about 0.2 second duration and 150 volts amplitude is applied with the electrodes held firmly against the ventricles. If the fibrillation is not arrested, the shock is applied again with two or three rapid volleys each of three to five shocks. If unsuccessful, massage is repeated, and the voltage may be increased before another attempt is made. In a series of thirty-nine defibrillation tests using this procedure in dogs, normal heart action was restored in thirty-five cases. Defibrillation was almost invariably successful if applied immediately after the onset of ventricular fibrillation in a healthy heart. Care should be taken, in defibrillating, not to have intracardiac pacemaker electrodes in the immediate current path.

Shocks of 110 volts at 25 cycles per second and 110 volts direct current were not effective in arresting fibrillation, in our experiments. Facilities were not readily available for use of higher voltages in either case, so these tests are not conclusive.

In most of these tests, fibrillation was induced by application of 5- to 20-volt shocks of 60-cycle per second sinusoidal current. A 20-volt square wave shock at 100 cycles per second was substituted in one instance, and produced fibrillation. Current outputs from laboratory oscillators were insufficient for defibrillation using square waves or pulse wave forms.

CLOSED-CHEST DEFIBRILLATION

Intracardiac Electrodes.—An attempt has been made to develop a closed-chest technique. The first approach was to pass a defibrillating current through a modification of the intracardiac catheter electrodes as they lay in various positions in the right atrium and right ventricle. Shocks of 1.0 to 3.2 amperes and 0.2 second duration were applied.

Six experiments were conducted with these intracardiac electrodes. Only partial defibrillation resulted. In every case but one, fibrillation persisted about the apex, and it was found impossible to reach this extremity of the ventricles with the shock. In each instance there was an area of burnt tissue around the electrodes after three or four shock applications. The one exception was a 10-kilogram dog whose heart was defibrillated on the fifth attempt, with a current of 2.4 amperes after 2.5 minutes of fibrillation.

In one animal, square waves and monophasic and biphasic pulses were tried at 140 volts (open circuit) and at frequencies from 25 to 400 cycles per second, without success. Here again, current output from available oscillators was limited. Shocks of 110 volts of 25-cycle per second current or of direct current also failed to defibrillate.

Intracardiac and Chest Electrodes.—A second technique used a single electrode catheter in the heart and a large dispersive electrode on the front of the chest, over the apex of the heart. This electrode arrangement was designed to extend the shock over a wider ventricular area. Shocks were applied between the catheter electrode and the dispersive plate.

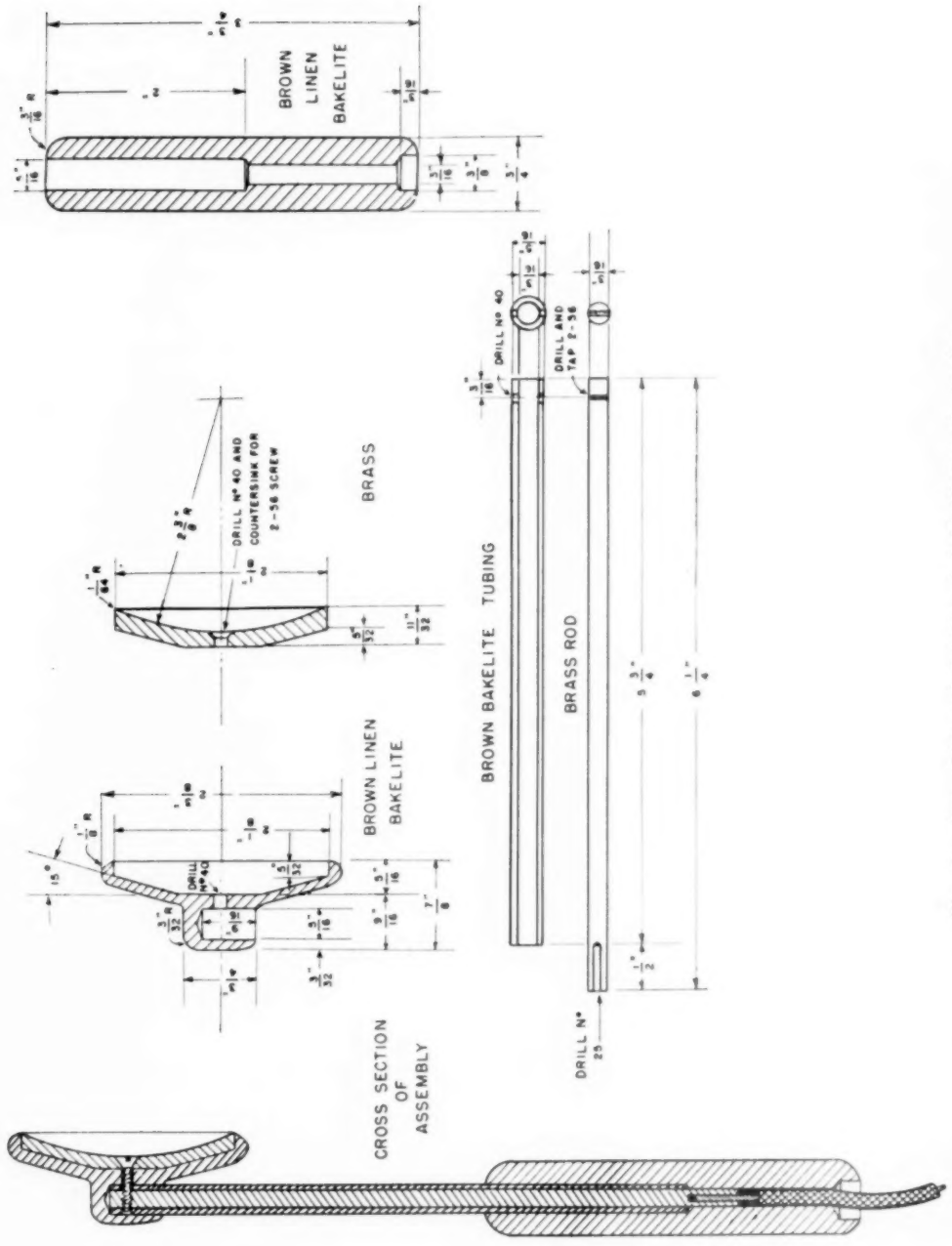


Fig. 6.—Assembly and details of defibrillator electrodes.

The results are shown in Table I. The technique proved fairly satisfactory in five of the eleven dogs tested. On analyzing our results, there appeared to be a definite relationship between the size of the dog and our ability to defibrillate. This has been our impression using the conventional method of defibrillation. With a larger dog, the greater size of heart and increased current path undoubtedly contribute to the difficulty of defibrillation.

TABLE I. EXPERIMENTS IN INTRACARDIAC-CHEST DEFIBRILLATION

EXPERIMENT NUMBER	WEIGHT (KG.)	NUMBER OF DEFIBRILLATIONS ATTEMPTED (1-6 SHOCKS)	NUMBER OF SUCCESSFUL DEFIBRILLATIONS (INTRACARDIAC TO CHEST)	MAXIMUM DURATION OF FIBRILLATION (BEFORE SHOCK APPLICATION) (MIN.)	VOLTAGE	CURRENT (AMP.)
1	8.3	9	7*	6	150-230	—
2	18	2	0	3	250	—
3	11	4	3*	5	250	3.6
4	15	2	0	2	260	3.5
5	10.5	5	5	2.5	120-170	1.8-2.4
6	22	2	0†	17	400	3.9
7	15	2	0†	9	440	—
8	14	2	0†	6	360	—
9	10	2	2	2.5	440	3.9
10	21	1	0†	5	420	—
11	12	2	2	3	440	4.0
Totals		33	19			

*With chest exposed, see text.
†Chest subsequently opened and fibrillation arrested with disk electrodes after massage.

In two of the tests, the first attempts to defibrillate were unsuccessful, and it was necessary to open the chest, massage, and defibrillate with conventional electrodes before performing further tests with atrium-chest electrodes. Subsequent defibrillations by this method did not constitute valid tests under closed chest conditions.

No attempt was made to duplicate Kouwenhoven's closed-chest method of defibrillation using two external electrodes, although in one instance a hypothermic dog was defibrillated by passing 135 volts of 60-cycle per second current from one side of the chest to the other. Current was not recorded. A 6-month-old infant was recently defibrillated at a body temperature of 21° C. by this method. Normal heart action continued. Consequently the chest was opened and the operation completed.

THE COMBINED STIMULATOR-DEFIBRILLATOR

For laboratory use, stimulator and defibrillator circuits have been combined in one instrument, illustrated in Fig. 7 and shown schematically in Fig. 8. The stimulator circuit has a single impulse switch for manual operation, and a neon indicator lamp for checking the pulse rate.

The defibrillator includes a timing circuit which limits the shock duration to 6.7, 10, or 20 cycles, corresponding to one-ninth, one-sixth, and one-third second. An indicator lamp glows for the duration of shock application.[8]

For hospital use, the combined unit has been simplified to reduce the number of required controls. The voltage and shock duration controls for defibrillation are located inside the cabinet, and panel manipulation is limited to adjustment of pulse rate and voltage, and selection of stimulating or defibrillating outputs. The unit has a pulse output amplitude variable in two decades from 0 to 10 or from 0 to 100 volts. The defibrillator voltage output can be set at 170 or 220 volts. The equipment is illustrated in Fig. 9, and the circuit shown in Fig. 10.

Fig. 7.—A stimulator-defibrillator with electrodes attached. The unit illustrated has a modified stimulator output circuit, giving 20 volts maximum. Output impedance is 500 ohms.

We have found 1.6 amperes to be a minimum current, and 2.0 to 3.5 amperes to be dependable current values for defibrillation. In a dog, the resistance across the heart measures about 55 ohms; hence, a practical voltage range is from 110 to 165 volts.

In all our experimental investigations, the use of a cathode-ray electrocardiograph has been invaluable for continuous observation of heart activity. For the experiments in closed-chest defibrillation, the addition of a muting switch to the electrocardiogram permitted quick recovery of the trace after shock applications, so that the effect of the shock could be observed.

DISCUSSION

The stimulator or artificial pacemaker has been used successfully for cardiac standstill upon experimental animals. One seldom encounters accidental car-

diac arrest at normal body temperatures during experimental surgery unless it is a result of cardiac anoxia, where the pacemaker is ineffective. A heart in standstill at normal body temperature would require good oxygenation and muscle tone with rapid filling on massage before the stimulator would work. These conditions have not been encountered experimentally, except in standstill created by vagal stimulation, where the pacemaker is effective.

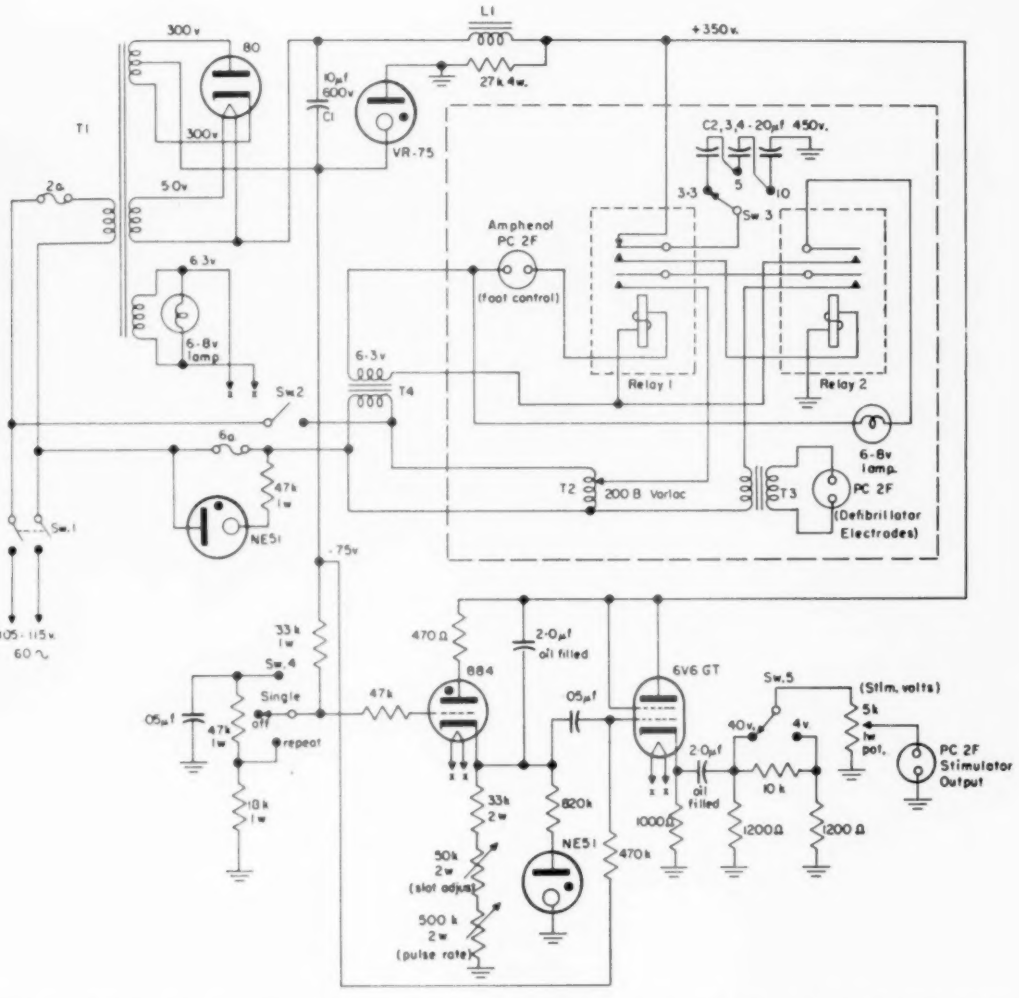


Fig. 8.—Schematic diagram of a stimulator-defibrillator, with 50-volt, 1,000-ohm impedance stimulator output.

The stimulator has proved very effective experimentally for standstill at low body temperatures. If there has been a delay in applying the pacemaker, then cardiac massage should first be used to ensure oxygenation and muscle tone.

This device has been available in the operating room for three years, but it has not had as yet a satisfactory or successful clinical trial. Its value may prove to be limited to the standstill of hypothermia.

The defibrillator, on the other hand, has proved equally successful at low body temperatures as well as normal body temperatures, and experimentally as well as clinically. When countershock therapy is applied for ventricular fibrillation, it does not make any difference, within limits, how long the heart has been fibrillating. The success of the defibrillation depends upon the state of the cardiac muscle, as evidenced by muscle tone and vigor of the fibrillation contractions. Without cardiac massage, defibrillation must be carried out within one to five minutes at normal body temperature with a correspondingly longer period of grace in hypothermia.

Fig. 9.—Clinical model of the stimulator-defibrillator.

At normal body temperature, defibrillation should be successful one-half hour after onset of fibrillation in experimental animals and human beings, provided the circulation and cardiac muscle tone have been maintained by cardiac massage and drugs. Dr. Callaghan[11] successfully defibrillated a patient seventy minutes after onset of cardiac arrest using the device described previously. We have had other successful cases of shorter duration.

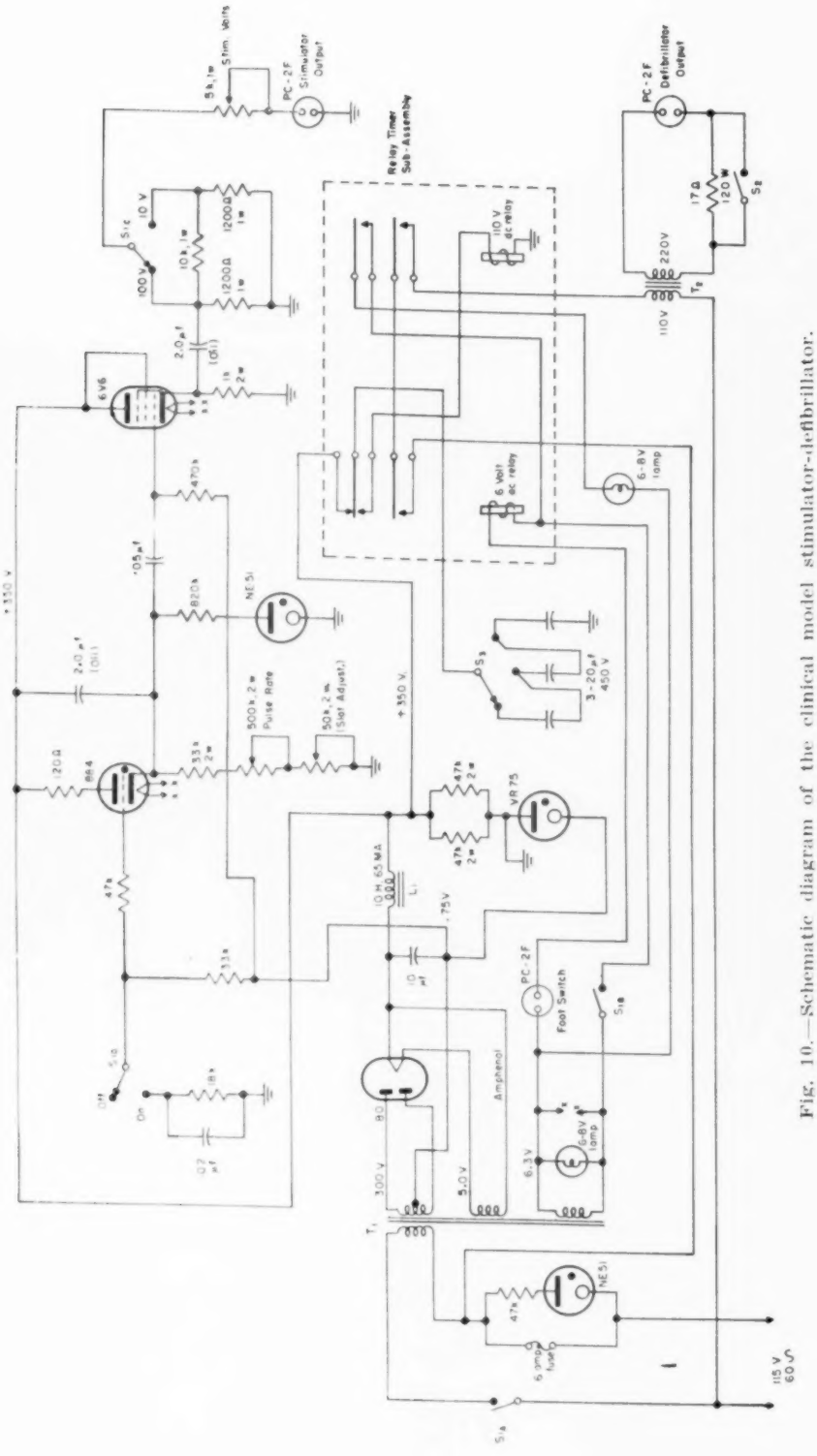


Fig. 10.—Schematic diagram of the clinical model stimulator-defibrillator.

The combined stimulator-defibrillator unit has been used clinically in this center for three years. The stimulator should be available in operations where hypothermia is used, but in ordinary surgery at normal body temperature, it is still in the investigation stage.

SUMMARY

1. The design and function of an electric artificial pacemaker for cardiac standstill have been described. It is principally effective at low body temperatures. When applied to the normally beating heart at normal body temperatures, it may be used to control the heart rate.

2. Repetitive single pulses of two to three milliseconds' duration and a current of from 0.01 to 0.02 ampere are effective in pacemaker stimulation. Currents as high as 0.1 ampere have been used without inducing fibrillation.

3. The design of a defibrillator has been described which has been effective in converting ventricular fibrillation to normal cardiac action both at low and normal body temperatures, experimentally and clinically.

4. Currents from 1.6 to 3.5 amperes are suggested as suitable values for defibrillation. Shock application should be limited to a duration of 0.2 second or less to protect the ventricular muscle against the destructive effect of continuing high current passage.

5. Shocks applied through an intracardiac catheter were not effective in cardiac defibrillation. It was impossible to arrest the ventricular muscle around the apex by this method.

6. With a single intracardiac electrode and a dispersive electrode on the chest over the heart, closed-chest defibrillation was possible in smaller dogs. As in open-chest technique, there appears to be a relationship between the size of dog and the ability to defibrillate.

7. The pacemaker stimulator and countershock defibrillator have been combined in one unit for experimental and for clinical use. The defibrillator includes a timing circuit to limit the duration of shock application.

ADDENDUM

Since preparation of this report, an interesting application of cardiac stimulation has been reported by Zoll.[9] Using external needle electrodes in the fifth left intercostal space and fourth right intercostal space, he has applied sharp-rise, exponential-decay pulses across the ventricles to restore ventricular rhythm from standstill. Zoll suggested the possible use of our stimulator (Fig. 3) and of an instrument combining stimulator and defibrillator circuits. The clinical model of our combined instrument provides sufficient pulse amplitude for Zoll's method of stimulation. If a 1:2 ratio transformer is connected to the defibrillator output the instrument provides 440 volts for the closed-chest defibrillation technique of Guyton and Satterfield.[10]

Acknowledgments.—These experiments were conducted over a period of three years by Dr. J. C. Callaghan, Dr. John McBirnie, and Dr. F. G. Pearson. We are indebted to: Mr. Donald Hughes for his laboratory assistance; Mr. C. F. Pattenson of the National Research Council Laboratories for his technical guidance; and Mr. J. R. Charbonneau of the National Research Council, who constructed the equipment.

REFERENCES

1. Bigelow, W. G., Callaghan, J. C., and Hopps, J. A.: General Hypothermia for Experimental Intracardiac Surgery, Ann. Surg. **132**: 531, 1950.
2. Bigelow, W. G., Pearson, F. G., and McBirnie, J.: Cardiac Resuscitation. To be published.

3. Callaghan, J. C., and Bigelow, W. G.: An Electrical Artificial Pacemaker for Standstill of the Heart, Ann. Surg. **134**: 8, 1951.
4. Szent-Gyorgyi, A.: Contraction in the Heart Muscle Fibre, Bull. New York Acad. Med. **28**: 3, 1952.
5. Hooker, D. R., Kouwenhoven, W. B., and Langworthy, O. R.: The Effect of Alternating Electric Currents on the Heart, Am. J. Physiol. **103**: 444, 1933.
6. Wiggers, C. J.: Cardiac Massage Followed by Countershock in Revival of Mammalian Ventricles From Fibrillation Due to Coronary Occlusion, Am. J. Physiol. **116**: 161, 1936.
7. Beck, C. S., and Mautz, F. R.: The Control of the Heart-beat by the Surgeon, Ann. Surg. **106**: 525, 1937.
8. Hopps, J. A.: Electric Countershock Treatment of Ventricular Fibrillation, National Research Council of Canada, Report No. ERB 267.
9. Zoll, P. M.: Resuscitation of the Heart in Ventricular Standstill by External Electric Stimulation, New England J. Med. **247**: 768, 1952.
10. Guyton, A. C., and Satterfield, J.: Factors Concerned in Electrical Defibrillation of the Heart, Particularly Through the Unopened Chest, Am. J. Physiol. **167**: 81, 1951.
11. Callaghan, J. C.: Personal communication.

Appraisal of Progress in Surgical Therapy

CONDUCTED BY WARREN H. COLE, M.D.
ASSISTED BY
J. GARROTT ALLEN, M.D. CLARENCE DENNIS, M.D.

THE ROLE OF GASTROINTESTINAL DECOMPRESSION IN SURGERY

JOHN R. PAINE, M.D., BUFFALO, N. Y.

INTRODUCTION

TWENTY-TWO years have passed since Wangensteen[7] described the treatment of patients with simple mechanical obstruction of the small bowel by continuous suction applied to an indwelling duodenal tube. One year later the indications for this type of treatment were extended to include patients with paralytic ileus and postoperative distention.[6] These papers stimulated in the surgical profession a wide interest in the possible benefits resulting from intestinal decompression which continues up to the present time. During the intervening years, this method of therapy has been critically appraised. The principles on which it is based have been universally accepted. There remain, of course, differences of opinion as to just how and when it should be used. A variety of suction tubes have been developed in an effort to improve on technique and to increase the usefulness of the method. The end result has been to improve the results of surgery, particularly abdominal surgery. Of the many factors which have made surgery safer and less disagreeable during the past generation, this greater emphasis on intestinal decompression is one of the more important ones. Gone are the days when the treatment of intestinal obstruction was accompanied by a mortality of 40 to 50 per cent. Gone are the days when the surgical house officer had to lavage repeatedly the stomachs of his patients following major surgical procedures performed within the abdomen.

It is, therefore, perhaps not inappropriate to attempt to evaluate the role of intestinal decompression in present-day surgical practice.

MECHANICAL AND PHYSIOLOGIC RATIONALE OF DECOMPRESSION

As initially employed by Wangensteen, the principle of applying a mild, continuous suction to an indwelling tube was limited to decompressing the stomach of a patient with severe peritonitis following the perforation of a peptic ulcer. Following an exploratory laparotomy and closure of the perforation, a gastrostomy was constructed and a catheter inserted into the lumen of the stomach. Constant suction applied to this catheter, minimizing the ab-

Received for publication, May 6, 1954.

dominal distention, together with other supportive therapy was thought to be the reason why this patient in 1931 survived for seven weeks before succumbing to the infection.

During the next few weeks, the principle of maintaining a constant suction in the upper gastrointestinal tract was employed in the treatment of three patients with simple small bowel mechanical obstruction. In these patients a Levin duodenal tube was inserted through the nose. In each instance the obstruction relented without the necessity of operative intervention. These happy results seemed to confirm the importance of continuous intestinal decompression by suction applied to an indwelling tube. Extensive clinical trial of this method of treatment was carried out at the University of Minnesota Hospitals during the next two or three years, and simultaneously the method was tested experimentally in the laboratory.

It was definitely shown that if constant mild suction was maintained on a tube inserted into the stomach, the distention of the gastrointestinal tract incident to paralytic ileus from any cause could be almost entirely prevented, provided the treatment was begun before the distention had developed. This is easily understood when it is remembered that about 80 per cent of the gas content of the bowel comes from swallowed air. Any means that removes this swallowed air from the stomach before it passes through the pyloric sphincter will prevent intestinal distention.

The removal of gas and fluid already in the small intestine or colon by means of a suction tube was recognized to be an entirely different problem. When suction was applied to a tube inserted into the stomach, the removal of any gas and fluid beyond the pylorus was dependent upon the regurgitation of such material into the stomach by means of reverse peristalsis. In the presence of a paretic or paralyzed bowel, this does not occur to any appreciable extent. In the presence of simple mechanical obstruction of the small bowel, however, reverse peristalsis is quite active so that in many patients an adequate decompression of the bowel proximal to the obstruction may be accomplished even though the suction tube remains in the stomach. In any event a more effective decompression of the bowel can be obtained if the point of suction can be advanced into the bowel by the passage of the tube through the pyloric sphincter and on down the intestine. It was for this reason that a number of modifications of the duodenal tube have been developed. The types most frequently used are the Miller-Abbott,[5] the Cantor,[1] and the Levin.[4] Likewise, a great amount of time and effort has been spent in attempts to devise a method by which a tube can be made to pass out of the stomach and into the duodenum quickly and consistently. Gastric peristalsis, magnetism, gravity, and mechanical force by means of a stylet directed under fluoroscopic control have all been utilized in the efforts to solve this problem. There are probably individual surgeons and investigators who believe that their method or regimen provides the ideal solution, but for the profession as a whole, this problem remains as the chief difficulty in the everyday use of intestinal decompression.

Even when the duodenum has been intubated, however, and the intestine plumbed to any desired depth, a new problem is immediately presented. This

is the necessity of maintaining suction simultaneously in the stomach and bowel if distention is to be prevented from recurring in the proximal portion of the gastrointestinal tract as the more distal portion is decompressed and emptied of its content. To meet this difficulty, when a long intestinal tube is employed, a second tube must be inserted into the stomach, or the long tube must be constructed with a double lumen which decreases its efficiency because of the narrower lumen. Furthermore, the necessity of placing the side openings in the tubes at a fixed point strictly limits the usefulness of any such tube. It was with an understanding of these difficulties that Wangensteen and Paine[5] modified

Fig. 1.—Types of gastrointestinal tubes most frequently used.

A, Miller-Abbott tube: This is a long tube with a double lumen. Balloon at leading end is partially distended with air or water after pylorus has been passed to increase its speed of passage through the intestinal tract by peristalsis.

B, Levin duodenal tube: This is a relatively short, smooth, tipped tube with openings for aspiration at its leading tip.

C, Modified Levin duodenal tube: This tube is the same as *B* except that the tip has been weighted by the incorporation of lead in the rubber and by extending the aspiration openings back from the leading tip so that aspiration can be maintained simultaneously in both the stomach and duodenum.

D, Cantor tube: This is a long, single-lumen tube for intestinal intubation. The balloon at the leading tip is partially filled with mercury. This by its weight and volume increases the ease and speed of intubation. The aspiration openings are relatively large.

the Levin duodenal tube to provide it with a smooth, weighted tip and side openings extending back about nine inches from the tip as the best practical compromise. With this tube, the duodenum can be intubated with reasonable facility in most patients, and suction can be maintained simultaneously in both the stomach and small bowel through a lumen of relatively large size. In my opinion, this is still the best tube for general use. There is no reason, however, why any surgeon should not use that tube which gives him the best results.

Because the ileocecal sphincter permits increments of gas, fluid, and solid bowel content to pass into the cecum but prevents their passage in the reverse

direction, all attempts to decompress the distended colon by means of an intestinal tube, no matter how long, will prove unsuccessful unless the tube can be made to traverse the entire length of the bowel and enter the cecum. A given amount of distention can be prevented in large measure from becoming greater, but relief from distention already present must be secured by operative means. There may be the occasional patient with an incompetent ileocecal sphincter in which some degree of decompression of the colon can be achieved by decompressing the small bowel, but the results will be slight and are not to be depended upon.

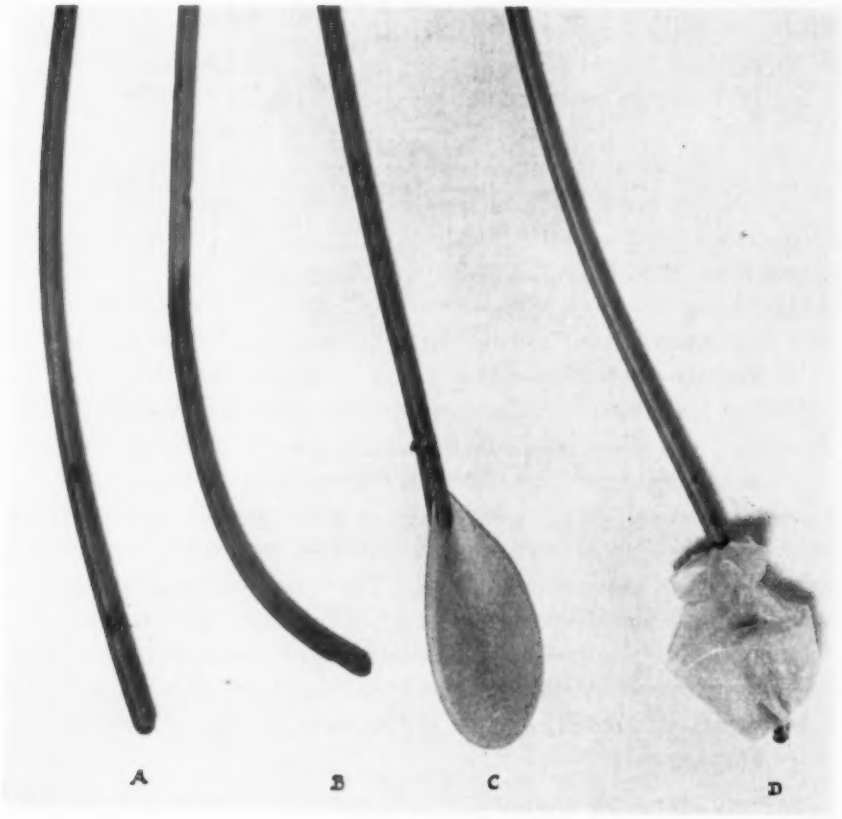


Fig. 2.—Enlarged view of decompression tubes showing the details of the leading tips.
A, Levin duodenal tube.
B, Modified Levin duodenal tube.
C, Cantor intestinal tube.
D, Miller-Abbott intestinal tube.

USE OF GASTROINTESTINAL DECOMPRESSION IN CLINICAL SURGERY

Constant mild suction applied to an indwelling duodenal or intestinal tube is employed in modern surgical practice in the treatment of two clinical entities: (1) intestinal obstruction and (2) paralytic ileus.

INTESTINAL OBSTRUCTION

Small Bowel.—For many years prior to 1931 surgeons had known that patients with an adhesive or inflammatory obstruction of the small intestine frequently were entirely relieved of the obstruction after the proximal bowel was

decompressed by an enterostomy. It was the knowledge of this fact that first gave Wangensteen courage to attempt the nonoperative treatment of such patients by decompressing the proximal bowel through an indwelling tube. A high degree of success was obtained, but this was achieved only by the careful selection of patients to exclude instances of strangulation and infarction, by constant close observation on the part of the attending surgeon with frequent x-ray examinations of the abdomen, and by a diligent effort on the part of attentive house officers to see that the minutiae of care were properly attended to. Going through the motions was not enough. In hospitals where these basic principles of care are not available, the nonoperative treatment of intestinal obstruction should not be attempted.

Even in our best hospitals, however, there are certain reasons why the nonoperative method of treatment is not used as much as it might be. The most important of these is the difficulty, and at times the impossibility, of distinguishing between a strangulated and a simple obstruction. The patient with an infarcted segment of intestine is no less of a surgical emergency because he has an indwelling tube inserted into or through his stomach and is being injected with the most modern and potent antibiotic drug on the market. An additional reason is that most hospitals nowadays are lacking in a sufficient number of interns and residents with the interest required to give the patient with obstruction treated by suction the amount of care and observation he requires. Even the best of nursing care is not a proper substitute for this. Finally, the risk of operating upon the patient with intestinal obstruction today is much less than it was twenty years ago. Anesthetic techniques now permit the induction and anesthetization of a patient with a minimum of risk from aspiration and other complications. Muscular relaxation can be secured without producing a dangerous depth of anesthesia. Satisfactory methods by which the dilated obstructed bowel can be safely handled and immediately decompressed at operation are much better understood. Incomparably more effective methods for preventing and treating infection are available. For these reasons the advantages of avoiding definitive surgical procedures in the distended obstructed patient have become less.

Despite the decreased emphasis which today is placed on intestinal decompression as a definitive means of treating patients with obstruction, all patients in which this diagnosis is suspected should immediately have a decompression of the gastrointestinal tract begun by the insertion of an indwelling tube through the nose into the stomach. The type of tube employed is of secondary importance as long as the stomach is emptied and kept empty. Further distention will be prevented, decompression of the bowel will begin if reverse peristalsis is active, and the patient's abdominal symptoms will be greatly relieved. At this point the surgeon must decide on the basis of his physical examination and laboratory procedures, including a roentgenologic examination of the abdomen, whether or not the patient is to be operated upon as soon as he can be adequately prepared by the administration of any indicated blood or parenteral fluid or is to be subjected to a trial of nonoperative treatment by intestinal decompression.

For those patients on whom immediate operation is planned, it is probably best, if the abdominal distention is only moderate, to be satisfied with a decompression of the stomach while the other preoperative preparations are being completed. Reasonable attempts, however, to secure some further degree of decompression can be made by causing the patient to lie on his right side and advancing the suction tube gradually in the prospect of intubating the duodenum. It would not seem worth while, however, to complicate matters by making a strenuous effort to do this by the use of any special maneuvers or complicated apparatus. Especially is this true in those cases in which the presence of strangulation or infarction is suspected. In these instances, hours are precious.

In that large group of cases, however, in which the obstruction appears to be, without doubt, simple in character, a different attitude may be taken. In these patients an immediate operation is not imperative and, if necessary, twenty-four to forty-eight hours can be reasonably used in an effort to secure an effective decompression of the proximal bowel. If this can be successfully accomplished, operation will not be necessary in many of these patients.

What means are employed to achieve decompression in this situation will depend on various factors such as the amount of time and care that can be given to the patient, available facilities for frequent roentgen examination of the patient's abdomen in following the progress of treatment, and the surgeon's own enthusiasm or preference for the use of a particular intestinal decompression tube. I must confess that I have never been convinced that the results obtained by using the longer tubes, such as the Miller-Abbott or the Cantor tube, are worth the increased amount of time, effort, and bother which their proper use demands, as compared to the results obtained by the shorter Levin tube with weighted tip. It must be admitted, however, that intestinal decompression can probably be accomplished somewhat more frequently and more rapidly if the leading end of a long tube can be made to negotiate the pyloric sphincter and work its way down the bowel while an additional tube is provided to keep the stomach empty.

Whatever means are employed to decompress the bowel, it is probably not wise to persist in this method of treatment for more than forty-eight hours without resorting to operation. Admittedly this is an arbitrary time limit and should be varied according to the circumstances of the individual case. A change in the clinical picture suggesting the development of infarction will demand immediate operation. On the other hand, a progressive decompression, although slow, may justify the continuance of conservative treatment beyond forty-eight hours. Experience has shown that if an adhesive obstruction relents at all with decompression, it does so in the great majority of cases rather quickly. If operation must be resorted to, its postponement for longer than forty-eight hours frequently brings on complications which increase the risk of surgery. The effects of starvation can only be decreased, not eliminated, by the most energetic of parenteral feeding. Changes in the bowel wall both proximal and

at the point of obstruction incident to prolonged distention and the pressure of an adhesive band or some other obstructing mechanism increase the hazard of the inevitable handling of bowel.

In my own practice, patients with small bowel obstruction are managed as follows:

Patients with strangulation obstruction, with infarction of the intestine, or patients in whom these conditions are suspected: Decompression of the stomach with a modified Levin duodenal tube is started immediately. While other preoperative preparations are carried out, an attempt is made to intubate the duodenum by having the patient lie on his right side and slowly advancing the tube inch by inch every few minutes. Operation, however, is not postponed for this purpose. Suction is maintained on the tube during the operation and afterward until the bowel has recovered sufficiently to function in an effective manner. This usually requires three to four days.

Patients with simple small bowel mechanical obstruction: The modified Levin-type tube is inserted into the stomach, and an attempt is made to cause it to pass into the duodenum by positioning the patient and slowly advancing the tube at intervals. An anterior-posterior x-ray film of the abdomen is taken every twelve hours to check the position of the tube and the change in the gas pattern of the bowel. The patient's abdomen is examined more frequently to determine whether or not signs of strangulation have developed. At the end of forty-eight hours, if a successful decompression with restoration of the continuity of the bowel lumen has not occurred, as evidenced by the passage of flatus or the change in the gas pattern on the roentgenogram, the patient is operated upon electively. Suction is maintained on the indwelling tube, however, as indicated previously.

Large Bowel.—The role of intestinal decompression by means of an indwelling tube in patients with obstructions of the colon should be confined to preventing as much as is possible the distention of the colon which is already present from becoming greater. This is done by removing from the stomach all swallowed air and any fluid which may be ingested, secreted, or regurgitated before these substances have had an opportunity to pass down the intestinal tract and enter the cecum. For this purpose, the use of a modified Levin-type duodenal tube inserted into the stomach which may or may not enter the duodenum is all that is required. In some patients a long intestinal tube can be made to traverse the entire small bowel and enter the cecum where decompression may become effective. The dangers inherent in the delay occasioned by the attempt to do this are real, and the effectiveness of the decompression achieved through the small lumen of the tube becomes less as the character of the bowel content becomes more formed. An adequate decompression of the colon must be achieved by operation. The choice of surgical procedure to be used for this purpose lies between a colostomy in the transverse colon and a cecostomy. Which procedure is used will depend on the location of the obstructing lesion and the training and practice of the surgeon. I believe that whenever possible a colostomy in the transverse colon is preferable to a cecostomy.

Here again decompression of the proximal portions of the gastrointestinal tract should be maintained by continuous suction throughout the period of operative treatment.

PARALYTIC ILEUS

The best definitive treatment for the clinical syndrome known as paralytic ileus is the application of constant suction applied to a tube inserted into the upper gastrointestinal tract through the nose or mouth. The surgeon must contend daily with paralytic ileus in his patients as the normal consequence of major procedures performed within the abdomen. This condition occasionally accompanies operations performed outside the abdomen and frequently follows major trauma of any sort. It is universally present at least in some degree in all patients with peritonitis.

The patient with paralytic ileus has an intestinal tract with diminished muscular tone and with weak or absent peristaltic movements. The bowel is incapable of transporting its contents in a normal fashion. The continuing addition of air swallowed into the stomach together with secretions from the stomach and duodenum which gradually work their way down the gut produces a progressive distention.

The insertion of a suction tube into the stomach of such a patient will immediately empty this organ. With peristalsis diminished or absent, however, very little regurgitation from the duodenum occurs, and the effect of the suction on the distention of the intestinal tract as a whole is slow to manifest itself and slight in degree. Nevertheless, such treatment will largely prevent the distention already present from becoming greater. This in itself is of great benefit to the patient. If the progressive character of the distention can be stopped, the smooth muscle of the bowel wall can better accommodate itself to the bowel contents, with normal muscle tone and peristaltic movements returning much sooner than would otherwise be the case.

If an attempt is made to employ a long tube and intubate the small bowel for a more effective decompression, greater difficulties will be encountered than in the patient with intestinal obstruction. The relative lack of any movement of the stomach and small bowel furnishes but little force to propel the tube, even though the pyloric sphincter itself may be passed.

It is, therefore, obvious that it is much easier and effective to treat the distention of paralytic ileus in a prophylactic fashion than to wait until it is full blown before decompression is started. It is not usually difficult for the experienced surgeon to know fairly well after examining a patient with acute abdominal symptoms or at the time of operation whether or not an appreciable degree of ileus is likely to follow. If more than a minimal amount is anticipated, decompression of the gastrointestinal tract should be begun at once. Maintenance of suction on an indwelling tube confined to the stomach is all that is required. The modified Levin duodenal tube with suction holes extending back from the leading tip some nine inches is the best tube to employ. It can be inserted with the least amount of discomfort to the patient, and if it should pass into the duodenum, suction will still be maintained within the stomach

as well. This type of treatment should be continued until the bowel has demonstrated its recovery of normal function. Such a situation, perhaps, is best judged by noting the repeated spontaneous expulsion of flatus by the patient, but this may not occur for twelve to twenty-four hours after other tests indicate that decompression is no longer required and that the indwelling tube can be removed.

The maximum comfort of the patient should never be forgotten. Despite the best of care, the presence of a tube inserted through the nose into the stomach and maintained in place for a relatively long time is never relished by anyone. In order to be able to remove these tubes as soon as conditions will permit, the abdomen should be auscultated with the stethoscope at least twice a day to detect the return of normal peristaltic sounds. When in the observer's opinion these can be heard at fairly frequent intervals, the patient's ability to get along without decompression should be tested before the suction tube is removed. Despite the discomfort of keeping the tube in place, this is usually less than the discomfort and discouragement which are occasioned by reinserting it once it has been removed. For such a test, the tube should be clamped for four hours and the patient required to drink two glasses of water during this time. If at the end of this four-hour period the patient has not become distressed or distended, or has not vomited and, when the tube is unclamped, if no more than a couple of ounces of fluid is immediately aspirated, the tube can be removed without further concern.

Although peritonitis from any cause is much less frequent today than in years gone by, it is still a problem of such magnitude as to merit the surgeon's greatest concern. The two elements of the modern treatment of peritonitis which have made the greatest contribution to better results now achieved are: (1) the antibiotic drugs and (2) continuous decompression of the gastrointestinal tract. The benefits of decompression arise from its effective control of the paralytic ileus, which is almost always associated with the infection and in its severity parallels that of the infection. Such should be continued until the bowel has regained its ability to function in a normal manner. Decompression secures the greatest amount of physiologic rest for the inflamed bowel that can be obtained. It will promote an increased flow of blood through the bowel wall by minimizing the pressure within the lumen. These effects, in turn, tend to limit the spread of the infection, shorten its duration, and prevent secondary adhesive intestinal obstruction, as well as enhance the comfort of the patient.

If decompression is to be employed after an operation, it is best to have the tube inserted through the nose and suction begun about one hour before the patient goes to the operating room. This will give the best possible assurance against aspiration of gastric contents by the patient during the induction and course of anesthesia. Suction should be continued throughout the course of the operative procedure. Keeping the stomach collapsed and empty facilitates all operations carried out in the upper abdomen and eliminates all risk of aspiration in the immediate postoperative period. In certain hypersensitive individuals and in patients unable or unwilling to cooperate in having an indwelling tube

inserted, the surgeon will do well to wait and insert the tube after anesthesia has been induced. Under such circumstances, most patients become accustomed to the presence of the tube during the immediate postoperative period, when sedation is fairly well marked, and tolerate it very well.

It is impossible to state categorically exactly which operations produce a sufficient degree of paralytic ileus to make intestinal decompression a worthwhile part of their treatment and which do not. The degree of response to trauma manifested by the individual patient varies a great deal. Certain general rules can be given, however. Few, if any, surgeons routinely employ decompression of the gastrointestinal tract prophylactically after operation other than abdominal operations. A significant amount of paralytic ileus may occur after intrathoracic procedures and other operations of long duration, but such instances are rare. Good postoperative care will detect the signs of ileus before the picture is fully developed in the occasional patient, and decompression can be begun immediately.

In general it can be stated that all patients undergoing a surgical procedure which involves a wide opening of the peritoneal cavity or more than a minimal disturbance of the abdominal viscera will profit by the use of intestinal decompression in the postoperative period. There are, no doubt, many surgeons who will disagree with this statement. The opposite position which might be taken would be to recommend the use of intestinal decompression after surgery only in those patients who manifest a distinct need for it. The actual role of decompression in modern surgical practice probably lies somewhere between these two extremes. I believe, however, that as a rule intestinal decompression is still used too little rather than too much.

Each surgeon, in judging for himself just how important a role decompression should play in his practice, should not forget that the effective control of postoperative distention and vomiting has purposes other than that of contributing to his patient's comfort. Judiciously used, this method of treatment gives excellent protection to the healing anastomotic suture line in the stomach, small bowel, and colon. In many clinics it has superseded the use of a proximal enterostomy after small bowel resections and a proximal colostomy after large bowel resections. Clinical observation has demonstrated that the incidence of postoperative obstructions due to adhesions is much less frequent if distention is prevented by gastrointestinal decompression in the immediate postoperative period. Furthermore, any means by which the disrupting strains on the healing wound of the abdominal wall incident to vomiting and distention can be diminished will decrease the frequency of wound dehiscence and evisceration.

It is generally agreed that inguinal herniorrhaphies and uncomplicated appendectomies are usually associated with such a mild degree of paralytic ileus that the routine use of intestinal decompression is not justified. In that large group of patients subjected to operative procedures on the biliary tract, however, the greatest variation is seen in the use of this therapeutic method. Even in the same clinic or hospital no uniformity of opinion on the matter exists. Certain members of the surgical staff of my own hospital never employ decompression unless forced to by the development of a progressive distention and the associated

profuse and continuing vomiting. I must admit, however, that I am unable to perform any type of biliary surgery without producing in my patients so consistently such a degree of paralytic ileus that I employ intestinal decompression routinely after this type of operation. Although occasionally perhaps unneeded, its routine use seems to be the wisest course to follow, and in the over-all results much more good than harm is done by its use. There is almost universal agreement that decompression is routinely indicated in the postoperative care of patients having resections of the stomach and bowel or any abdominal operation of a similar or greater magnitude. A considerable degree of variation exists with respect to its use postoperatively in patients having operations performed upon the organs within the pelvis and upon the urinary tract. A short period of decompression is probably indicated in most cases.

In many hospitals, when suction through an indwelling tube is employed, there is a great tendency to discontinue it arbitrarily after a certain length of time, which is frequently too short. Each patient should be individualized and decompression discontinued only after a proper trial, as described previously. The time required for patients to recover from a postoperative ileus is two to four days. In those patients whose convalescence is complicated by a peritonitis, the time may be appreciably longer.

COMPLICATIONS OF GASTROINTESTINAL DECOMPRESSION

The use of suction applied to various types of tubes inserted into the stomach or through this organ into the intestine for the purpose of gastrointestinal decompression is associated in a small percentage of patients with a variety of complications. Most of these complications occur as the result of ignorance of the limitations of the method or the improper use of the suction tube. Disturbance in the fluid and electrolyte balance of the patient is by far the most frequent complication seen. The surgeon must never forget that variable but relatively large amounts of gastric and intestinal secretions are continually being removed. Due allowance must be made for these daily losses and the deficits made up by replacement through parenteral fluid administration.

The other complications are directly related to the prolonged presence of the tube in the nasopharynx and upper gastrointestinal tract. In most instances they are pressure phenomena. Kleinsasser[4] in 1951 summarized very well the complications reported in the literature up to that time. The more important of these are as follows:

1. Abscess of the nasal septum.
2. Sinusitis and otitis media.
3. Ulceration of the larynx, occasionally resulting in stenosis.
4. Ulceration of the esophagus, occasionally resulting in stenosis.
5. Rupture of esophageal varices.
6. Perforation of the esophagus, stomach, and small bowel.
7. Knotting of the tube within the stomach or intestine.
8. Inability to withdraw the balloon-tipped tube.

The more serious of these complications have resulted from a lack of care and gentleness when the tube was inserted or from maintaining the tube too long

in one position before withdrawing it. This type of complication, although uncommon in any series of cases, can be further minimized if, in those cases in which decompression must be long continued, the suction tube is withdrawn and reinserted through the opposite side of the nose every five or six days. It should be noted in passing that the majority of reported complications have occurred in patients being treated with one of the several types of long intestinal tubes.

SUMMARY

During the past twenty years, the beneficial effects of gastrointestinal decompression have been recognized and accepted as an important part of surgical therapy. Experience has shown that it is much easier to prevent distention of the gastrointestinal tract by suction applied to an indwelling tube than to relieve a distention already present. Various types of tubes have been developed in an attempt to obtain more effective and quicker decompression of the small bowel. Ideally, gastrointestinal decompression should be obtained by maintaining an effective suction simultaneously in both the stomach and small bowel. An acceptable practical solution to this problem is not available at present.

Gastrointestinal decompression has been found to be particularly useful in two clinical entities: (1) intestinal obstruction and (2) paralytic ileus. As a definitive means of treating patients with simple small bowel obstruction without operation, it has an important but somewhat limited role. In general, these limitations depend upon the difficulty in distinguishing with certainty between simple and strangulation obstructions and the time and care necessary for the use of the method. As an essential part of the surgical treatment of all cases of obstruction, decompression should be used routinely. In obstructions of the colon, decompression by means of an indwelling tube is ineffective except that it will, to a great extent, prevent a distention already present from becoming greater. Decompression of a distention already present must be secured by operative means.

The greatest benefits of gastrointestinal decompression have come from the effective control of the distention and vomiting associated with paralytic ileus. This method of treatment is most effective when used in a prophylactic fashion. Considerable differences of opinion exist as to its exact role in postoperative care. In general, it is indicated in the treatment of all patients undergoing major abdominal surgical procedures and particularly in those patients having operations upon the gastrointestinal tract or in the treatment of any patient in whom more than a minimal degree of ileus can be expected to follow operation. This form of therapy should be an essential part of the treatment of any patient with peritonitis. Associated with control of distention and vomiting, decompression protects the patient against the bronchial aspiration of gastric contents, encourages the adequate and rapid healing of intestinal suture lines, minimizes the incidence of abdominal wound dehiscence and evisceration, and decreases the incidence of postoperative adhesive obstruction.

Complications associated with the use of gastrointestinal decompression are rare if this method of treatment is properly used and its limitations understood. Disturbance of fluid and electrolyte balance is the most common and important.

REFERENCES

1. Cantor, M. O.: New Simplified Intestinal Decompression Tube, Am. J. Surg. **72:** 137-142 (July) 1946.
2. Cantor, M. O.: Intestinal Intubation, Springfield, Ill., 1949, Charles C Thomas, Publisher.
3. Kleinsasser, L. J.: The Complications of Gastric and Intestinal Intubation, Am. Pract. & Digest Treat. **2:** 221, 1951.
4. Levin, A. L.: New Gastroduodenal Catheter, J. A. M. A. **76:** 1007 (April 9) 1921.
5. Miller, T. G., and Abbott, W. O.: Intestinal Intubation: A Practical Technique, Am. J. M. Sc. **187:** 595-599 (May) 1934.
6. Paine, J. R., Carlson, H. A., and Wangensteen, O. H.: Post Operative Control of Distention, Nausea and Vomiting; Clinical Study With Reference to Employment of Narcotics, Catharties and Nasal Catheter Suction-Siphonage, J. A. M. A. **100:** 1910-1917 (June 17) 1933.
7. Wangensteen, O. H.: Early Diagnosis of Acute Intestinal Obstruction With Comments on Pathology and Treatment, With Report of Successful Decompression of Three Cases of Mechanical Bowel Obstruction by Nasal Catheter Suction Siphonage, West. J. Surg. **40:** 1-17 (Jan.) 1932.
8. Wangensteen, O. H.: Intestinal Obstruction, ed. 2, Springfield, 1942, Charles C Thomas, Publisher, chap. 6, p. 157.